



# Surgery, Gynecology and Obstetrics

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# SURGERY, GYNECOLOGY AND OBSTETRICS

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## PHYSIOLOGICAL RESPONSES OF TRANSPLANTED PROSTATIC TISSUE IN THE ANTERIOR CHAMBER OF THE EYES OF RABBITS<sup>1</sup>

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From the Thompson Urological Fund of Rush Medical College, University of Chicago

Of the many experimental methods used for the study of autotransplantation of tissue the anterior chamber of the eye as a situs has been found to be of particular value to observe the physiological and anatomical changes. The earlier investigators did not fully appreciate the possibilities of this location as an ideal place for normal tissue growth but recently many authors have found the anterior chamber of the eye to be a suitable place to study the normal physiological responses of transplanted tissue.

In 1873 VanDooremaal transplanted the mucous membrane of the lip into the anterior chamber of the eye, and discovered a tendency toward cyst development in the transplant. Goldziehr followed with his report on the results of transplanted nasal membrane in 1874 and in 1890 Hanseemann recorded the transplantation of embryonic tissue. From that time on until early in the twentieth century it appears that little work of importance was accomplished.

Foremost in the recent literature are the names of Schochet, Neumann, Litt, Allen, Bauer, Priest, Podleschka and Dworzak. These investigators, using principally the female sex organs, showed the comparative ease with which endometrial tissue will grow when transplanted to the anterior chamber of

the eye. This situs is ideal because it offers excellent visibility for observation of the tissue, a good circulation for the transplant to grow, and provides easy recovery of the tissue for microscopic study.

For these reasons, it occurred to us that some constructive information could be obtained if pieces of the prostate gland were transplanted into the anterior chamber of the eye.

In this study, 20 male rabbits were used in varying ages from 8 to 12 months. Under ether anesthesia, the abdomen was opened by midline incision. The bladder was emptied by manual decompression and pulled up and out of the abdomen and retracted posteriorly. With an Ellis clamp, the seminal vesicles were grasped and pulled upward and then held in place by an assistant. The large bowel was freed as far down as possible from the base of the bladder and held down with a small sponge. The two arteries running upward along the outer border of the prostate and seminal vesicles were ligated low down near the neck of the bladder. This later technique, which was developed only recently in the course of the experiment, controlled to a great degree the bleeding and hemorrhage and made the process of enucleation of the prostate easier.

<sup>1</sup>Read at meeting of the North Central Urological Society, Cleveland, Ohio, November 8, 1934.

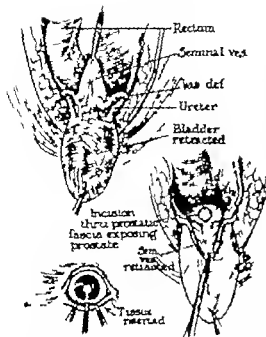


Fig. 2. Technique used in removing the prostate and inserting the piece into the eye. *a*, Incision at incision. A small piece of prostatic tissue being inserted underneath the cornea.

The prostate could now be distinctly seen beneath the fascia as a yellow mass. A mid line incision was made through the fascia and with a pair of forceps and a pair of small

scissors the prostate was enucleated from its bed and detached low down at the neck of the bladder. Great care was taken in order not to injure or squeeze the tissue. A small pack was then placed in the prostate bed for a few minutes to control the hemorrhage and then removed.

Several pieces of prostatic tissue not more than  $\frac{1}{4}$  millimeter square were then cut from the prostate and placed in a warm normal salt solution.

The eye was then prepared for the transplant by clipping the lid hair with an ordinary finger nail scissors. No antiseptic solution was used in the eye. With two small forceps with teeth, the eye was grasped near the limbus and slightly rotated upward. An incision 5 millimeters long was made through the cornea at the limbus with a cataract knife. Sufficient fluid usually escaped so that the intraocular tension was decreased enough to allow the implant to be easily inserted with the aid of a blunt spatula. No attempt was made to close the incision with catgut and the eye was left open. After a little practice the pieces could be inserted without a great deal of difficulty.

In presenting our results a composite picture of the group is used rather than the gross and microscopic findings in each case.

A successful growth was obtained in 36 of the 40 eyes. Of the successful transplants 10 became infected and were discarded. This is



Fig. 1

Fig. 1. Prostatic mass 6 weeks after it had been transplanted.

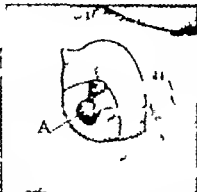


Fig. 3

Fig. 3. Transplant of prostatic tissue before injection of anterior pituitary like hormone.



Fig. 4

Fig. 4. Marked increase in the size of the transplanted prostate following administration of anterior pituitary like hormone is shown. *A*, Prostate; *B*, small cystic areas in prostatic tissue.



Fig 5 Low power microscopic section of transplanted prostatic tissue A, Cornea B, Iris C, Anterior chamber D, Note the attachment of one piece of prostatic tissue to the cornea

the most important complication. The eyes of each rabbit were enucleated, under ether anesthesia, from 2 to 10 months after the prostate was transplanted, the rabbit was then immediately killed and autopsy performed.

The eyes were at once placed in Mueller's solution and left in this solution for 3 weeks, changing to fresh fluid several times. Then they were washed in running tap water for several hours, placed in a solution of 10 per cent formalin for 24 hours, and again washed in tap water. Each eye was run through 70 per cent, 80 per cent, 95 per cent, and 100 per cent alcohol for 24 hours, then removed from the alcohol and a window light opening about 1 centimeter square was cut in the back. Following this, it was put into a solution of absolute alcohol and ether for 24 hours, after which time the iris was removed. The eyes

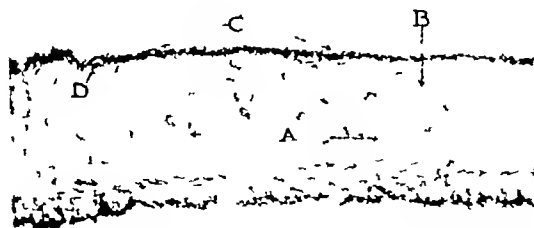


Fig 7 Section of iris showing tendency of the prostatic tissue to proliferate along the surface A, Iris B, Anterior surface C, Proliferation of glandular prostatic tissue along the surface of the iris D, Tendency to form glandular structure See Figure 8



Fig 6 High power view of D in Figure 5 Note normal structure of prostatic tissue.

were then placed in thin celloidin for 5 weeks, into a thick solution of celloidin for several days, then blocked, labelled, and put in 80 per cent alcohol until ready for use.

When the tissue was cut, each section was placed on previously numbered small filter papers, thus keeping the serial numbers in proper order of cutting. These sections were kept covered at all times with 80 per cent alcohol. The usual standard staining methods were employed.

In our experiment, 850 sections were stained and studied.

From 12 to 14 hours after the prostatic tissue was placed in the anterior chamber, the eye showed a marked reaction as from a foreign body. There was profuse excretion and the conjunctiva was congested and red. A marked congestion of all the vessels at the limbus took place. Usually this acute reaction



Fig 8 High power view of region D in Figure 7 A, Tendency of cells to form glandular structures



Fig. 9. Low power microscopic view of prostatic tissue after stimulation with anterior pituitary-like hormone. A. Cornea. B. Iris. C. Anterior chamber. D. Marked hyperplasia of the glandular structure.



Fig. 10. Microscopic view of another section of prostate gland transplant after stimulation with anterior pituitary-like hormone. A and B. Formation of large cystic spaces. C. Marked glandular hyperplasia.

subtended by the ninth day and definite dilated blood vessels could be seen centering about and entering into the transplanted tissue. During the next 3 to 4 weeks, in some of the eyes, there was an increased ocular pressure. From 6 to 8 weeks changes were observed which we were able to interpret only after the eyes had been studied microscopically.

This finding was the appearance of small cystic spaces which grossly had a gray tinge varying from the size of a pin head to 5 millimeters in diameter. The microscopic structure of these epithelial lined cysts will be illustrated in the slides. These cysts did not cause any abnormal reactions.

Another interesting microscopic finding was the proliferation of a layer of columnar cells

over the anterior surface of the iris on to the cornea. This epithelium was directly continuous with, and similar to the glandular structure of the prostatic cells. (Fischer and Ebeling have shown experimentally in tissue culture that epithelium has the ability to form a delicate and continuous layer over the surface of artificial media.)

In those portions nearest the implant, it was high columnar and at the periphery the cells were often cuboidal. Many times this epithelium had the tendency to reproduce glandular structures resembling the original glandular structure of the transplant. This occurred always on the anterior surface of the iris and cornea and did not invade the stroma of these two structures.

To extend our experiment further a small group of rabbits were given daily injections of the anterior pituitary-like hormone and another group daily injections of antuitrin. These injections were started 10 to 12 days after the transplant and continued from 6 to 8 weeks. In those that had received the antuitrin, no noteworthy changes either macroscopically or microscopically could be seen. However important gross and microscopic changes were observed in some of the eyes of the rabbits that received injections of the anterior pituitary-like hormone.

From the seventh to tenth day following the first injection the transplant increased in size



Fig. 11. High power view taken from C in Figure 10. Note marked proliferation of gland tissue across of cells four or five layers deep.

and continued to do so until in several of the eyes, at the end of 3 to 4 months they had covered one-half of the surface of the eye. Furthermore, it was observed that in the gross anatomical changes there was a marked increase in the vascular supply to the transplant characterized by an increase in the number and size of the blood vessels. In the transplant itself there were many large translucent gray areas.

In the study of the micropathology, the following changes were observed. The formation of large cysts which corresponded grossly to the gray translucent areas. These cysts were similar to those which are frequently observed in the microscopic picture of benign prostatic hypertrophy. The cells lining these cysts were usually cuboidal, in some instances they were completely flattened in character. The second important change were areas where the glandular structure had undergone marked hyperplasia and hypertrophy. In many sections the glandular epithelium was three to four layers deep with an increase in the papillary arrangement of these cells.

#### SUMMARY AND CONCLUSIONS

1. The results of the autotransplantation of the prostatic tissue in the eyes of rabbits are recorded.

2. Pieces of prostatic tissue were transplanted and grew when they were placed in the anterior chamber of the eye of the rabbit.

3. The tissue maintained its normal structure.

4. The glandular cells proliferated along the anterior surface of the iris and reproduced gland-like spaces.

5. The ease of transplantation, constant visibility, a fluid filled space for growth and nourishment and prompt vascularization lead us to believe that the anterior chamber of the eye is an ideal location for the study of transplanted prostate.

6. Preliminary observations from the use of the two pituitary-like hormones on the transplanted prostatic gland are given.

#### REFERENCES

- 1 ALLEN, EDWARD, and BAUER, CARL P. *Surg, Gynec & Obst*, 1928, 47, 329-333.
- 2 ALLEN, EDWARD, and PRIEST, FRED O. *Surg, Gynec. & Obst*, 1932, 55, 553-558.
- 3 GOLDZIEHR. *Arch. f. exper. Path.*, 1874, 2, 387.
- 4 HANSEMAN. *Arch. f. path. Anat.*, 1890, 119, 324.
- 5 LITT, S. *Am. J. Obst.*, 1933, 26, 36-44.
- 6 NEUMANN, R. *Arch. f. Gynaek.*, 1932, 150, 393-429.
- 7 PODLESCHKA, von DR. KURT, and DWORZAK, HANS. *Med. Klin.*, 1934, March 29, 438-441.
- 8 SCHOCHET, S. S. *Am. J. Obst.*, 1929, 17, 1328.
- 9 VAN DOOREMAAL. *Arch. f. Ophth.*, 1873, 19, 359.



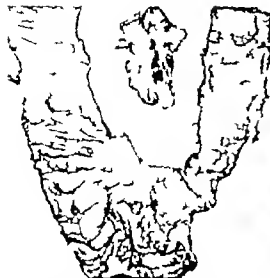


Fig. 1. Case 4. Terminal ileum, cecum, and proximal portion of colon. Note the swollen Peyer's patches, the ulceration of the ileum, the thickened ulcerated ileocecal valve, the marked edema of the mucosa of the cecum and the unobscured swollen solitary lymph follicles in both ileum and colon. The arrow shows a number of swollen mesenteric glands.

marked in the region of the ileocecal valve as to prevent the passage of gas or fluid through this aperture. The mucosa throughout of the lower part of the ileum was only moderately inflamed. The Peyer's patches stood out very prominently (Fig. 1). In places they were from 3 to 4 millimeters in thickness; the epithelium over them was ulcerated and was covered by a thick, shaggy grayish-white pseudomembrane. Some of the patches were surrounded by a narrow zone of hyperemia. Scattered between them were numerous swollen lymph follicles in the mucous membrane. Most of these had a yellowish, necrotic, umbilicated center. Some of these also were surrounded by a zone of hyperemia. In the distal 6 centimeters of the ileum, the ulceration became confluent, involving the bulk of the mucosa, which was completely covered by grayish-yellow shaggy pseudomembrane. The edematous thickening of the walls of the intestine was very marked in this region. Here the cut edge of the muscular portion of the wall had a pale grayish-white semi-transparent appearance. While the cut edges of the Peyer's patches were necrotic, dark red to grayish red. Removal of the pseudomembrane revealed a reddish granular surface. This membrane covered both proximal and distal surfaces of the ileocecal valve and extended into the cecum for a distance of about  $\frac{1}{2}$  centimeters. Beyond this point while the wall of the cecum and the proximal portion of ascending colon showed marked edema, the ulceration and pseudomembrane formation was confined to the solitary lymph fol-



Fig. 2. Case 4. Cecum. Erosions on surface of mucosa. Hemorrhage and foam stain, X30.

icles. Many of these were greatly swollen, raised above the surface of the surrounding mucosa. The unobscured crypts and were covered by a grayish-yellow membrane. Some of the smaller ones were surrounded by a zone of hyperemia. They were most numerous in the proximal 3 centimeters of the ascending colon with an occasional one near the hepatic flexure and one situated in the beginning of the transverse colon. The remainder of the large bowel appeared quite normal.

The liver weighed 460 grams. On gross examination it appeared congested, and the cut surface was somewhat green. The spleen weighed 34 grams. Its surface was smooth and dark red. The cut surface appeared healthy. The kidneys weighed, right 64 grams, left 55 grams. The surface was smooth, of brownish-red color and the arterial veins were rather prominent. The capsule stripped readily. The cortex and medulla appeared healthy. The ureters, bladder, suprarenals, and pancreas appeared healthy. Uterus, tubes, and ovaries were of the healthy size and type.

The anatomic diagnosis was acute pseudomembranous ulcerative ileocolitis. Acute inflammation of ileocecal valve with stuporous acute intestinal obstruction, acute mesenteric lymphadenitis, acute fatty liver, partial pulmonary collapse, early bronchopneumonia, thrombosis of central vein, congestion of kidneys.

**Microscopic examination.** Section taken through the ileocecal valve and adjacent ileum and cecum showed the greater part of the mucosa to be ulcerated and covered with a thick layer of exudate composed of necrotic cells, fibrin, few erythrocytes, and numerous colonies of bacteria (Fig. 2). In gross stained sections these bacteria proved to be gram-negative bacilli. Here and there a few islands of epithelial cells still remained, but these stained poorly and showed varying degrees of necrosis. The lymphoid tissue had undergone marked necrosis. In places the greatly swollen Peyer's patches and sol-



Fig 3 Case 4 Edge of Peyer's patch Note the great depth of tissue between the muscularis mucosae and the muscle coat, also the thick overhanging exudate on the surface of the mucosa. Hematoxylin and eosin stain,  $\times 30$

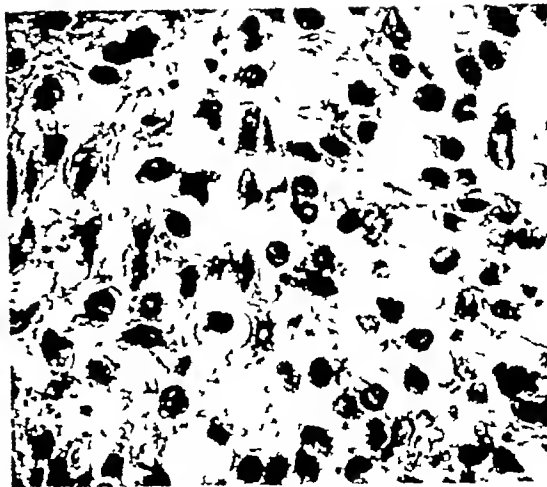


Fig 4 Case 4 Photomicrograph of submucosa of terminal ileum, showing the type of cellular reaction Note the scarcity of polynuclear cells Hematoxylin and eosin stain  $\times 685$

tary lymph follicles remained as only necrotic shadows of their former structure, with here and there a few intact lymphocytes around their periphery (Fig 3). One interesting feature was the comparative absence of polymorphonuclear leucocytes in the presence of such marked necrosis, such extensive fibrin formation, and such enormous numbers of bacteria. While a few leucocytes were seen usually close to the mucosal surface, many of these had pyknotic nuclei. The infiltrating cells in the wall were sparsely scattered and were made up for the most part of large mononuclear cells with oval, pale staining vesicular nuclei (Fig 4). These were interpreted as endothelial leucocytes. There were also scattered lymphocytes. Another striking feature was the degree of edema particularly in the submucosa. This extended throughout the cecum and up the ascending colon, well beyond the areas of ulceration. It was this edema rather than the cellular infiltration which accounted for the marked increase in thickness of the wall of the colon (Fig 5).

Many of the solitary lymph follicles also showed necrotic centers with ulceration of the overlying epithelium, giving the follicle a crater-like structure. This appearance was accentuated by the presence of a thick, fibrinous, necrotic membrane which was adherent to the rim of the crater and overhung its edges (Fig 6). Sections stained for amebas according to the technique recently described by Meriwether were negative. The muscular portion of the wall appeared to suffer less severely than the other structures. In places it showed little change, while in those regions corresponding to the most extensive epithelial damage, there were varying degrees of intercellular edema, with infiltration with a few mononuclear cells. The muscle fibers themselves did not appear to be seriously damaged. In the subserosa

also were varying degrees of edema and sparse cellular infiltration, while the serous surface for the most part appeared to escape. In only a few places could one see thin deposits of almost acellular fibrin on the serous surface. The blood vessels, on the whole, appeared to suffer but little. No change was noted in the arteries and arterioles. Some of the veins, however, particularly those adjacent to the more extensive necrotic areas were filled with thrombi, and in these regions too there were small areas of perivascular hemorrhage. The majority of the lymphatics

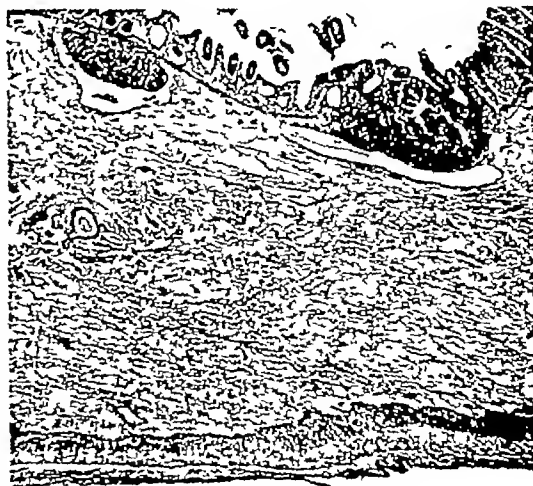


Fig 5 Case 4 Section of colon. In lower part of field whole thickness of muscular portion of wall is shown. Between this and the muscularis mucosae is the extremely edematous submucosa. Hematoxylin and eosin stain,  $\times 30$

while all of the 6 cases showed slight agglutination with a known motile *Bacillus coli*, no agglutination was obtained with the sera of another control group of 7 patients against a known strain of *Bacillus coli*.

These results might be interpreted as meaning that *Bacillus W* was the causative organism that agglutinins against that organism were produced in 4 of the other 6 cases tested, that the organism is closely related to the colon bacillus and for this reason there is some "group agglutination" with an ordinary strain of *Bacillus coli*. That this is the correct interpretation is by no means established. The series of cases as well as that of the controls is altogether too small to permit of any definite conclusions. Much more work remains to be done.

The lesson, it is true, bears a certain resemblance to that seen in some types of bacillary dysentery. In dysentery however the disease is usually more widespread. The cellular infiltration is greater, hemorrhages are more pronounced, the edema is less marked and what is of much greater significance is the fact that the patients have frequent bowel movements. In the cases reported here diarrhea was conspicuous by its absence. This, in view of the degree of inflammation is difficult to explain.

Clinically the disease has been repeatedly mistaken by us for acute appendicitis. To our knowledge there are no differentiating points in the history, physical examination, or laboratory findings. Postoperatively it has been noted that the increased temperature has returned to normal very slowly.

Thus far we have failed to find in the literature any detailed reports of a similar condition. That the disease is closely related to that variously described as regional ileitis, chronic ulcerating enteritis, or benign granuloma of the intestines we have great reason to believe. Increasing numbers of case reports under the headings mentioned are finding their way into the literature (1 & 4). The majority of the patients are adults and have come under observation when the disease has reached a chronic stage. In some the condition has simulated malignancy and attempts have been made to indicate its benign

nature by the use of such terms as benign granuloma of the intestines or inflammatory tumor of the intestines. Undoubtedly there have been included within this group conditions of varying etiology but recently Crohn, Ginsburg and Oppenheimer have attempted to separate what they believe to be a specific clinical entity which they have designated as "regional ileitis." This condition is defined by them as "a disease of the terminal ileum affecting mainly young adults, characterized by a subacute or chronic necrotizing and ulcerating inflammation. The ulceration is associated with a disproportionate connective tissue reaction of the remaining walls of the involved intestine, a process which frequently leads to stenosis of the lumen of the intestine associated with the formation of multiple fistulas. The disease is clinically featured by symptoms that resemble those of ulcerative colitis, namely fever, diarrhea and emaciation leading eventually to an obstruction of the small intestine, the constant occurrence of a mass in the right iliac fossa usually requires surgical intervention (resection). The terminal ileum is alone involved. The process begins abruptly at and involves the ileocecal valve in its maximal intensity tapering off gradually as it ascends the ileum orally for from 8 to 12 inches. The familiar fistulas lead usually to segments of the colon forming small tracts communicating with the lumen of the large intestine. Occasionally the abdominal wall anteriorly is the site of one or more of these fistulous tracts."

If the condition which we have described represents the early acute stage of what these observers designate as regional ileitis, it at once becomes obvious that the definition given requires some modification. The majority of the cases reported by these authors were young adults, the oldest patient being 52 and the youngest 17. If as is believed the process is an inflammatory one there would appear to be no reason why children should be immune. The ages in our series were as follows: 8½ years, 10 years, 3 years, and 2½ years. The detailed pathological findings are from the youngest case.

Of greater difficulty of reconciliation is the location of the lesion. Thus according to

Crohn is the terminal ileum. He states "in this disease the rectum and colon are never involved." If this statement is correct then the condition which we have described is obviously not one of regional ileitis. In none of our cases was the disease confined to the terminal ileum. In each instance there was some involvement of the cecum or colon. It should be pointed out, however, that in all 4 cases not only was the evidence of disease much greater in the ileum than in the colon but that all of our cases were seen during the acute stage while in all of the cases in which Crohn and his co-workers had an opportunity to study resected material "the patient had been ill for at least a year." Is it not possible that in some of these patients during the acute stage there may also have been some involvement of the cecum?

A glance at Figure 1 is sufficient to show that the ulcerative process is much more marked in the ileum stopping almost abruptly at the ileocecal valve although the edema of the colon is very pronounced. It is therefore quite conceivable that resolution in the colon might proceed to completion while the inflammatory process in the ileum might be progressive. In this connection also we should like to draw attention to the statement of Crohn that "the familiar fistulas lead usually to segments of the colon forming small tracts communicating with the lumen of the large intestine." While such fistulous lesions involving the colon may usually commence as primary ulceration in adjacent coils of ileum that they never develop from lesions primary in the colon may be very difficult to establish so that the bald statement "that the terminal ileum is alone involved" is perhaps too sweeping.

Then too it should be pointed out that Harris, Bell, and Brunn in discussing the nomenclature of this disease also question the advisability of limiting the disease process to the terminal ileum. In one of their reported cases, and in another not described in detail the lesions "involved mainly the jejunum." They therefore suggest the more inclusive term of "chronic cicatrizing enteritis" and express the belief that with "more universal recognition by surgeons of this disease process

other cases will be reported involving the jejunum as well as the terminal ileum." The same we believe may be said of the cecum and colon. However, while the name suggested by Crohn appears to be too limited, that suggested by Harris may on the other hand be too comprehensive. Recently under the title of "chronic cicatrizing enteritis" Donchess and Warren report a case with involvement of the entire cecum and ascending colon in a woman of 62 years, and present a synopsis of 24 other reported cases in which there is involvement of both cecum and colon. That these cases should all be included here is a question. While all may have shown a chronic cicatrizing process in some part or other of the intestinal tract yet some of them (including their own reported case) appear to have been secondary to appendicitis. That such a condition should follow acute appendicitis with extension of the inflammatory process to adjacent cecum and colon is not inconceivable, but is this the condition that Crohn is attempting to isolate from what he calls the "hodge-podge or melting-pot" in which are thrown all those benign inflammatory intestinal tumors which are neither neoplastic nor due to a specific bacterial agent? We think not. So that by whatever name this condition ultimately comes to be known care must be taken that it be not too restrictive on the one hand or too comprehensive on the other hand.

Clinically another apparent discrepancy requires consideration. According to Crohn one of the symptoms of "regional ileitis" is diarrhea, this was conspicuously absent in all our cases except in Case 3 in which fluid movements were noted following the administration of milk of magnesia. Here again let us point out that most of Crohn's patients "had been ill from several months to 2 years before coming under observation" and very little is known or recorded of the symptoms in the earlier course of the disease. It is quite conceivable that as the disease progresses and ulceration and cicatrization become more marked a chronic diarrhea might develop while inquiry into the history of these patients at the time of their acute illness might reveal the fact that diarrhea was not always a constant feature.

In the more acute cases to which Crohn refers, the findings as noted at operation are almost identical with what we have observed. In speaking briefly of the early phases of the disease he states the latter (that is the early phases) are sometimes encountered at the operating table following an illness of from 1 to 2 weeks and diagnosed as a rule as acute appendicitis. At this time the terminal ileum is found thickened, soggy and edematous, the serosa is a blotchy red. The mesentery of the terminal ileum is greatly thickened and contains numerous hyperplastic glands. Owing to the possibility of spontaneous resolution resection has never been performed at this stage so that we have no knowledge of the intra-intestinal changes present at this time.

Unfortunately he does not state whether any of these patients were followed and whether their subsequent history was in any way similar to that of the chronic cases which he describes. If however they do represent the acute stage of the disease, the striking similarity between his description and our own observations at least suggests that we are dealing with the same condition. If this assumption is correct then the description of the intra-intestinal changes during the acute stage of the disease which we have been fortunate enough to observe in Case 4 and which we have described in some detail, should add further to our knowledge of this subject. As for our non fatal cases, these will be followed with interest and will be reported upon at a later date.

In the meantime it is thought advisable to place our findings on record in the hope that further interest in this disease, particularly in the acute stage, may be aroused and its true etiology recognized. If this disease is of infectious origin as we believe it is, the discovery of an etiological agent is much more likely to be made during the acute stage before there has been opportunity for widespread invasion by the normal flora of the intestinal tract. Conclusions based upon bacteriological investigation carried out during the chronic stage will probably be of little value.

#### SUMMARY

Four cases of acute ileocolitis with marked edema of the intestinal wall are reported one with postmortem findings. The clinical resemblance of this disease to acute appendicitis is pointed out. Its relation to "regional ileitis, or chronic ulcerating enteritis" is discussed and it is suggested that the cases reported here may represent the acute phase of this condition. Its etiology remains obscure.

#### REFERENCES

1. CROHN, H. M. *Surg Clin N America*, 933, 356.
2. CROHN, BRANT, B. GORDON, LEON, and GIBBY. *Intestine Glands* D. J. Am. M. Ass. 934, 99, 1243. (Because of the frequency with which these authors are referred to in the text, the name of only the first author will appear.)
3. DOWNES, JOSEPH C. and WARREN, SETH. *Arch Path*, 934, 8, 21.
4. HARRIS, F. VERN I. BELL, CLYDE H. and BRUNY, HAROLD. *Surg Gynec & Obst*, 935, 77, 697.
5. MEINWATER, L. S. *Proc Staff Meet Mayo Clin*, 1934, 9, 95.

## THE EXPERIMENTAL PRODUCTION OF EXCESSIVE ENDOMETRIAL HYPERPLASIA<sup>1</sup>

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**A**BNORMAL uterine bleeding occurring just before or during the menopause and in the absence of gross pelvic lesions is frequently associated with a notable hyperplasia of the uterine mucosa. In some instances the glands are so greatly dilated that we are accustomed to speak of microscopic sections of such an endometrium as having a "Swiss cheese" pattern. By most authorities the hyperplasia in question is attributed to an ovarian disturbance characterized by an over secretion of estrin in the absence of corpora lutea. Indeed Witherspoon advances a step farther and postulates that the unopposed action of estrin on the uterus results both in immediate endometrial changes characterized by hyperplasia and in more latent myometrial pathology in the nature of fibromyomatous neoplasms.

There is definite experimental evidence which favors the first part of this view. Thus Hofbauer concluded from his experiments upon guinea pigs injected with alkaline extracts of pituitary glands that the internal secretion of the ovary is essential for hyperplastic changes occurring in the upper part of the uterine mucosa the "functionalis." On the other hand he holds that the basal layer as judged by the response of this structure to repeated pituitary administration in ovariectomized animals is under the control of the anterior pituitary. Fluhmann has demonstrated an excessive production of estrin during the course of endometrial hyperplasia and has suggested the name "hyperestrinism" to describe the condition. Again Burch, Williams and Cunningham operating upon two patients for hyperplasia of the endometrium failed to find corpora lutea in the ovaries of either. However, a follicular cyst was present in the ovaries of both patients. The fluid aspirated from these cysts was injected into spayed mice and rats. The changes previously found in the endometrium of each patient were similar in many respects to those found

in the uterus of the experimental animals receiving the fluid from that patient.

In a second series of experiments Burch and his associates injected spayed rats and guinea pigs with varying amounts of estrin for an average period of 3 weeks, the daily average injection consisting of 25 rat units. A large percentage of the experimental animals showed characteristic cellular reactions of the endometrium as well as Swiss cheese dilatations of the glands. The microscopic appearances of the specimens were very similar to those of human hyperplasia of the endometrium. A further series of experiments was reported in which hyperplasia was brought about as the result of continued estrus produced by partial castration.

Definite experimental evidence that the unopposed and prolonged activity of estrin is capable of inducing a degree of endometrial hyperplasia sufficiently pronounced to warrant the designation "Swiss cheese hyperplasia" is up to the present available only for the guinea pig. The present paper is a report of the experimental production of this type of hyperplasia in two catarrhine primates the chimpanzee (*Pan satyrus*) and the sooty mangabey (*Cercocebus torquatus atys*).

### EXPERIMENTAL DATA

*a Chimpanzee* The experimental animal was an adolescent female that had been used in a study of the sexual skin (Zuckerman and Fulton, 1934). At the time of the experiment she was about 8 years old and though she had shown signs of ovarian activity (as judged by swelling of the sexual skin) for some 14 months, she had never menstruated. Bilateral gonadectomy was performed on September 20, 1933, the ovaries contained numerous small follicles, but no luteal tissue. Apparently the animal had never ovulated.

Between October 6 and October 28, 1933, estrin<sup>2</sup> was administered in gradually mounting doses until a total of 21,100 rat units had been injected. The maximum dosage given in a single day was 1000 rat units.

<sup>1</sup>The estrin preparations were very generously supplied by the Parke Davis Company through the courtesy of Dr. Oliver Kamm and by the Schering Corporation through the kindness of Dr. Gregory Stracrell.



Fig. Photomicrograph showing endometrium of chimpanzee at the end of course of injections of estrin totaling 30 rat units. X



Fig. Photomicrograph showing endometrium of monkey at end of course of estrin injections totaling 55,075 rat units. Note the superficial zone of degeneration, and the dilated glands. X40

The animal, which was in a poor and emaciated condition, sacrificed on October 25. The reproductive organs were immediately fixed, and the following is description of the uterus, fresh after sectioning as stained with Mayer's bismuth and eosin.

Cystic dilatation of the glands, such as numerous, is displayed at all levels of the mucosa, and is visible to the naked eye. The condition extending from the two horns of the pseudobicornuate fundus as far down as the isthmus. 3/4 of the glands are coiled and branched, and most are filled with secretion and cast off glandular cells. The surface epithelium is somewhat irregular, and not as tall as that of the glands, and its usually contracted nuclei are placed toward the free border of the cells. Some of the glandular epithelium is of a similar character with the nuclei lying near the cell margin, and the deeper parts of the cells occupied by pale staining globules. On the whole, however, the glandular epithelium is taller columnar type than the surface epithelium. In the deeper glands, the nuclei are more prominent than those nearer the cavity, and they are usually situated somewhat away from the free margins of the cells. In the dilated or cystic gland the epithelium is irregular in some places flattened, in others heaped. The appearances suggest that after degeneration or rupture of their lining cells, some of these glands may cystically discharge their contents into the cavity, and by rupture of the surface epithelium, this process accounting for some of the irregularities in the latter and perhaps also for some localized accumulations of homogeneous eosinophilic material that are to be seen in the subepithelial zone. The stroma is tightly packed except toward the cavity, where it is somewhat laxer. The muscular blood vessels are dilated, but there are no extravasations of blood nor can any of the stromal collections of homoge-

neous eosinophilic material be ascribed with a certainty to previous extravasations.

Cystic glands do not occur either in the isthmus, or in the cervical canal. In cross section the uterine lumen in the region of the isthmus has the shape of a six pointed star flattened from back to front. The epithelium of the surface of this part of the uterus equals in height and otherwise resembles that of the coiled glands, the nuclei lying toward the free margins of the cells, the cytoplasm of which is broken up into light staining globules. The epithelium of the cervical canal is similar in appearance but taller (fig. 1).

*b. Monkey (Cercopithecus leucon et al.)* The experimental animal, as a full grown male monkey, whose menstrual cycles had been followed for 3 years previous to course of estrin injections. The average length of the ten preceding cycles was 33 days (range 30 to 36). Estrin injections were begun on the 15th day of the eleventh cycle and given daily until total of 55,075 rat units had been administered, the maximum amount administered on single day being 1,000 rat units. Presumably as result of these massive doses of the follicular hormone, the next menstrual period did not appear when expected and the cycle prolonged itself for 53 days. On the fifty-third day the animal died after an abrupt illness which lasted ten days. Sections of the uterus were prepared and stained with Mayer's bismuth and eosin. The histological appearances are as follows.

*The uterine wall.* The greatest depth of endometrium in any part of the stained preparations is 5 millimeters. The muscular layers of the uterus appear healthy but the mucosa presents picture of unusual degeneration.

The superficial third of the endometrium is considerably degenerated and appears as a somewhat homogeneous vacuolated eosinophilic matrix sur-

bedded in which are stromal and epithelial cells in all stages of degeneration. Completely degenerated glands are also represented in this zone. The blood vessels of the area are intact, however, in spite of the degeneration of the tissues surrounding them. At no point in the uterus, which was sectioned at various levels, was any extravasation of red blood cells seen.

The surface epithelium is mostly intact, but the majority of the cells, which are arranged in a single layer, have undergone pronounced vacuolar degeneration. Very little is left of the cells in those places where this process has proceeded farthest, although the basement membrane remains intact even in such regions. The degenerated remnants of surface epithelium, and presumably of cells of the superficial third of the mucosa as well, can be seen in the lumen of the body of the uterus.

The degenerated superficial zone grades into more healthy basal endometrium, which has a tightly packed stroma.

The uterine glands are numerous, and are mostly straight. Many are dilated and slightly coiled, and some are even cystic. In the basal zone of the endometrium, the narrow, elongated, highly chromophilic nuclei of the glandular epithelium occupy the greater part of the cell bodies. The nuclei in more superficial zones are generally situated in the middle third of their cells, separated from the basal third by clear vacuoles, and from the free margins of the cell by granular eosinophilic cytoplasm. The basal vacuolation appears to represent degeneration and not secretion, it seems to be the first step toward the total disintegration of the cell bodies, the next being the vacuolation of the granular cytoplasm which lies superficial to the nuclei.

Cystic glandular changes are confined to the body of the uterus and do not extend beyond the isthmus. There is practically no degeneration in the cervical canal, the epithelium and glands appearing relatively healthy. In this region of the uterus, both the surface and the glandular epithelium is high columnar, and both the main uterine lumen and the glands, some of which are greatly dilated, are filled with mucus, in which are numerous leucocytes which can also be seen penetrating the cervical epithelium.

*The ovaries.* The ovaries of this animal were sectioned serially. They presented the typical appearance of ovaries removed from animals which have been treated with estrin. They were small, follicular growth had been retarded, and there was a great deal of follicular atresia. No functional corpora lutea were present, and the only remains of such tissue were old and degenerated corpora obviously belonging to cycles preceding the one in which the animal was injected with estrin (Fig. 2).

To our knowledge endometrial degeneration of the extent and character presented in this specimen has not before been described as accompanying the administration of estrin. The appearance of the tissues makes it un-

likely that the pathological appearance of the endometrium was due either to postmortem changes or to changes brought about in the preparation of the sections. It is possible that the change was due to the very large dose of estrin administered, and it is also conceivable that the degeneration was an accompaniment of the acute and brief illness that preceded the animal's death. Whichever may have been the case, the factors which brought about this picture of degeneration are immaterial from the point of view of this discussion. From our present point of view, the important fact is the existence in this mangabey of considerable endometrial hyperplasia as indicated by the numerous glands of the mucosa and more particularly by cystic dilatation. The extent of the latter change is not as great as that which is shown by the chimpanzee described. Nevertheless the amount of hyperplasia and glandular proliferation is far greater than has previously been described as following the injection of estrin into monkeys.

#### EVALUATION OF PREVIOUS EXPERIMENTAL WORK

With respect to previous experimental work upon Primates Edgar Allen injected a spayed *Macacus rhesus* over a period of 22 days with a total dosage of 1065 rat units of lipid and aqueous extracts of human placenta and of liquor folliculi from pig ovaries. At the end of the experiment the endometrial glands were extremely long and showed considerable coiling and branching in the tips next to the internal muscular layer. In a further series of experiments a total of 550 rat units of extracts from human placenta and from liquor folliculi of pig ovaries was administered to three ovariectomized monkeys over a period of 24 days. The animals were then killed on the first, third, and fifth days after the last injection. The uterine mucosa of the animals killed on the first and third days after the last injection was pearly white, spongy, and edematous. That of the monkey killed on the fifth day was in an early menstrual stage. Histological sections showed a typical early menstrual endometrium.

Robertson, Maddux, and Allen injected ovarian hormones into 4 ovariectomized adult



female monkeys. In 1 a total of 447 rat units of lipoid extract of human placenta in oil solution was administered over a period of 48 days. In the 3 other animals, the period of injection lasted from 24 to 27 days, and the total dosage ranged from 882 to 981 rat units. In 2 animals corpora lutea were also implanted. Two experimental menstrual periods followed the cessation of injections of the estrus producing ovarian hormone. Sections of the uteri showed typical menstrual endometria of the non-ovulating type. Three implants of recent human corpora lutea did not increase the growth of the endometrial glands beyond the interval stage. In all these studies endometrial hyperplasia did not proceed beyond the point characterized by long tubular glands.

As far as we are aware only Werner and Collier have studied the effect of estrin upon the human endometrium. These authors administered to 5 women previously subjected to bilateral ovariectomy a total dosage of 25,200 rat units of theelin over a period of 84 days. A histological examination of the curettings obtained following this treatment showed an increase in the amount of endometrial tissue and the presence of hyperplastic glands which were irregular in form and similar to the glands found in endometrial hyperplasia of the human uterus. The hyperplasia produced, however was far less than that manifested by the chimpanzee and mangabey which form the subject of this report and about the same as that induced in the studies on monkeys which are cited in the preceding paragraph.

As was noted in the introduction to this paper the lesion under discussion is generally believed to result from a disordered ovarian activity. Indeed in many patients who complain of menorrhagia and in whom a hyperplastic condition of the endometrium is found, corpora lutea are absent from the ovaries and in addition it is found that the ovaries present cystic changes. It is assumed therefore that the hyperplastic lesion of the endometrium is due to the unopposed action of estrin.

In this connection the investigations of Smith and Smith are of interest. These

authors found that progestin prepared according to the method of Corner and Allen causes the excretion of injected estrin in rabbits. In a further study upon 8 women, 4 of whom presented an amenorrhea 3 of whom were sterile, and 1 of whom was normal Smith and Smith concluded that as in rabbits, estrin is excreted only when the human organism has been exposed to the action of corpus luteum. In 2 of their patients 1 a woman who had been completely amenorrheic for 3 years, there was a  $\pm$  reaction on the twenty-fourth and twenty-eighth days of the cycle for the excretion in the urine of estrin given orally. In the second patient, who had had no menstrual flow since a pregnancy 2 years previously there was a consistently negative reaction for the excretion of estrin given orally. The results in both these cases were interpreted by Smith and Smith as indicating that no corpus luteum was present during the period over which these patients were tested. The results which were obtained by these authors also suggest that estrin is most effective in the absence of corpora lutea.

As noted herein corpora lutea are absent from the ovaries of many women in whom menorrhagia is associated with a glandular hyperplasia of the endometrium. This clinical finding, taken together with the investigations of Werner and Collier and those of Smith and Smith, and with the results which were obtained following the administration of 1,100 rat units of estrin to a castrated chimpanzee and of 33,675 rat units of estrin to a normal monkey support the hypothesis that the unopposed action of estrin plays an important role in the production of glandular hyperplasia of the endometrium.

#### SUMMARY

The present paper is a report of the experimental production of an excessive endometrial hyperplasia identical in all macroscopic and microscopic characters with the Swiss cheese hyperplasia of human pathology which occurred in a castrated adolescent chimpanzee following a course of estrin injections totaling 21,100 rat units and in a normal mangabey monkey after a course totaling 33,675 rat units.

## REFERENCES

- 1 ALLEN, EDGAR. Further experiments with ovarian hormone in ovariectomized adult monkey, *Macacus rhesus*, especially degenerative phase of experimental menstrual cycle. *Am J Anat.* 1928, 42 467
- 2 Idem. Reactions of immature monkeys (*Macacus rhesus*) to injections of ovarian hormone. *J Morphol. & Physiol.*, 1928, 46 479
- 3 Idem. The ovarian follicular hormone, theelin, animal reactions. *Sex and internal secretions*. Baltimore: Williams & Wilkins Co., 1932
- 4 BURCH, WILLIAMS, and CUNNINGHAM. The etiology of endometrial hyperplasia. *Surg, Gynec. & Obst.* 1931, 53 338
- 5 BURCH, WOLFE, and CUNNINGHAM. Experiments on endometrial hyperplasia. *Endocrinology*, 1932, 16 541
- 6 FLUHMAN. Hyperplasia of the endometrium and the hormones of the anterior hypophysis and the ovaries. *Surg, Gynec. & Obst.*, 1931, 52 1051
- 7 HOFBAUER. Concerning the etiology of hyperplasia of the endometrium. *Surg, Gynec. & Obst.*, 1931, 52 222
- 8 ROBERTSON, MADDUX, and ALLEN. Ovarian hormone effects in ovariectomized monkeys. *Endocrinology*, 1930, 14 77
- 9 SMITH and SMITH. Studies on the urinary excretion of estrin with special reference to the effect of the luteinizing hormone and progestin. *Am. J Physiol* 1931, 98 578
- 10 Idem. The excretion of estrin by women. *Am J Physiol*, 1932, 100 553
- 11 WERNER and COLLIER. The effect of theelin injections on the castrated woman. *J Am M Ass.*, 1933, 100 633
- 12 Idem. Production of endometrial growth in castrated women. *J Am M Ass*, 1933, 100 1466
- 13 WITHERSPOON. The interrelationship between ovarian follicle cysts, hyperplasia of the endometrium and fibromyomata. *Surg, Gynec. & Obst.*, 1933, 56 1026

EXPERIMENTAL STUDIES ON THE EFFECTS OF THE PERFORATION OF PEPTIC ULCERS<sup>1</sup>

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**T**HE following description of the condition that develops after perforation of a peptic ulcer is given by Hermann in his *Textbook of Surgery*

The symptoms of an acute perforation into the free peritoneal cavity begin with a sudden, agonizing epigastric pain, always associated with evidences of shock, and usually accompanied by vomiting. The pain, at first, is localized but soon becomes general. Pallor is marked, the face drawn, the skin cold, the respiration shallow, the abdomen retracted and of boardlike rigidity. The peritoneal insult is more sudden and violent than that caused by any but the most unusual instances of appendicitis and tenderness, sharply localized over the region of the ulcer, usually can be brought out. At first the temperature is subnormal, the pulse little elevated. In the face of such a clean-cut emergency, it would hardly matter that no earlier story of ulcer could be obtained. However, the disease is not always so plainly labelled. Perforation in the course of an alcoholic spree is confusing; perforation upon an empty stomach, though unusual, causes symptoms of comparative mildness, and some duodenal perforations closely simulate appendicitis. In these latter the duodenal content leaks out principally into the right abdomen, causing local tenderness and spasm. Thus there may occur epigastric pain, followed by pain, soreness, and muscular resistance in the lower right abdomen—a picture of appendicitis.

The experiments to be described in this paper were performed in an effort to find the factors which are responsible in the main for early severe signs and symptoms that follow the perforation of ulcers. Further studies were performed in an attempt to determine the mechanism by which the circulatory collapse takes place in order that the alterations might be compared with those that are obtained in experiments in which shock is produced by other means.

For purposes of this study it seemed inadvisable to produce a perforation of the stomach or duodenum, as this would have introduced the operation and the anesthetic as complicating factors. Also this method does not allow one to determine which of the fluids that escape into the peritoneal cavity are responsible for the ill effects. Therefore a con-

dition similar to that which is observed following the perforation of a peptic ulcer was produced by injecting singly or in various combinations the different upper intestinal juices as collected from other dogs.

## METHODS

Bile was obtained by cannulating the common duct after having ligated and divided the cystic duct. It was collected in a balloon which was attached to the dog by the method of Roux and McMaster. Pancreatic juice was collected in a similar way from a cannula that was placed in the main pancreatic duct after having ligated and divided the accessory duct by the method of Elman. The duodenal secretion was obtained by placing a cannula in a closed loop of the duodenum which had been freed of its bile and pancreatic connections. The continuity of the intestinal tract was restored by anastomosing the stomach to the jejunum. The secretion from the stomach was collected by making a closed pouch of the lower two-thirds of the stomach into which a cannula was placed. The upper portion of the stomach was then anastomosed to the jejunum.

The balloons in which the various secretions were collected were emptied daily into sterile containers. The fluids were tested as to sterility on blood agar plates.

The fluids were injected in varying amounts and in varying combinations into the peritoneal cavities of unanesthetized animals. Syringes of 20 cubic centimeter capacity and medium sized needles were used for the introduction. Alterations in the general behavior of the animals in the pulse rate and in the hematocrit readings were observed. In the experiments in which death occurred the appearance of the intraperitoneal structures was noted and the quality of the free fluid in the peritoneal cavity was determined.

In the experiments in which the effects on the circulation of the intraperitoneal injection

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of the various fluids were studied, determinations of the cardiac output, pulse rate, maximum and minimum arterial blood pressures, blood concentration, femoral and splenic arterial inflow rates, and the body temperature were performed. Morphine was used as the anesthetic in these experiments. After having performed the control determinations, varying quantities of bile or pancreatic juice or both were injected into the peritoneal cavity, and another set of studies was made shortly thereafter. Additional determinations were carried out at approximately hourly intervals throughout the course of the experiments.

The cardiac output determinations were carried out according to the Fick principle. The arterial blood was collected under oil from the femoral or carotid artery and mixed venous blood was obtained from the right heart. The determinations of the oxygen content of the blood were carried out with the Van Slyke-Neill apparatus. The oxygen consumption was measured with the Benedict spirometer. A cannula, which was placed in a femoral artery and connected to a mercury manometer, was used in determining the blood pressure. Maximum and minimum valves were used. Hematocrit readings were determined by the use of Van Allen tubes. The arterial inflow rates were performed by the method which was described by Bartlett and modified by Erlanger.

At the completion of the experiments, the animals were killed painlessly and autopsied. The intraperitoneal structures were examined and the quantity of free fluid in the peritoneal cavity was determined.

## RESULTS

I The effects of the intraperitoneal injection of the fluids on the general condition of the animals, the survival period, and the blood concentration.

All of the animals became ill following the introduction of rather large quantities of one or more of the upper intestinal juices. Vomiting usually occurred shortly following the injection. The animals appeared weak and there was usually an early and significant increase in the pulse rate. The condition then seemed to improve for a while as has been described

by Homans in instances of perforation in the human.

A The effects of pancreatic juice. Death did not occur in any of the 9 experiments in which uninfected pancreatic juice was introduced into the peritoneal cavity. The quantity that was injected varied from 11 to 39 cubic centimeters per kilogram of body weight. In most of the experiments, there was a moderate increase in the concentration of the red blood cells. No difference in the effects of pancreatic juice obtained shortly after the operation and that a week later was observed. Death occurred in 3 of the 4 experiments in which infected pancreatic juice was used. The quantity that was introduced varied from 10 to 20 cubic centimeters. The length of time separating the injection and death was less than 24 hours in 2 of these experiments and 3 days in the 1 remaining. A great deal of free fluid was found at autopsy in the peritoneal cavity.

B The effects of bile. The studies in which bile was used were more difficult to evaluate because the effects seemed to vary somewhat according to length of time elapsing between the operation in which the common duct was cannulated and the time at which the sample of bile for injection was collected. For example, the use of 11 cubic centimeters of bile per kilogram of body weight from a dog which had been operated upon 1 day previously resulted in death, whereas the giving of 20 cubic centimeters of bile per kilogram of body weight 6 days later from the same animal did not cause death. In other words, the bile becomes less toxic per unit of volume as the length of time separating the operation and the collection increases. For the first several days following the cannulation of the common duct, the bile is thick in consistency and it later becomes quite thin.

Nineteen experiments were performed in which the effects of the introduction of bile were studied. All of the animals appeared quite sick immediately following the injection and it was my impression that they were somewhat sicker than the animals in which corresponding amounts of pancreatic juice were introduced. In only 6 of these experiments had the operation on the animal from which

the bile was obtained been performed 4 days or less previously. The quantity of bile that was given per kilogram of body weight in the different experiments was 6.4, 11.0, 15.0, 15.0, 20.0, and 31.3 cubic centimeters. The only animal which died was the one in which 11 cubic centimeters per kilogram of body weight had been given and death occurred in 24 hours. The hematocrit reading increased from 41.0 to 61.7 per cent. Autopsy revealed the presence of 265 cubic centimeters of blood tinged fluid in the peritoneal cavity and a great deal of reddening of the structures there. A moderate increase in the hematocrit reading took place in the 5 remaining experiments in none of which death occurred.

That infection may be an important factor is illustrated by the results of an experiment in which organisms were introduced intentionally into bile that was obtained from an animal which had been operated upon 13 days previously. Death took place 40 hours following the introduction of this bile in the amount of 10 cubic centimeters per kilogram of body weight. As a control, it was found that the injection of 37 cubic centimeters per kilogram of body weight of uninfected bile from the same animal did not produce death. However the recipient of the bile appeared quite ill for the first 24 hours.

C. The effects of the injection of equal amounts of bile and pancreatic juice. Twenty two experiments were performed in which the effects of the injection of equal amounts of bile and pancreatic juice were studied. All of the animals appeared to be quite ill following the injection and there was an increase in the pulse rate and usually vomiting. There was very little change in the hematocrit reading in some experiments while a rather marked increase was observed in others.

Eleven of the 22 experiments will not be considered further because of infection of the bile or pancreatic juice or the elapse of too long an interval between the cannulation of the duct and the obtaining of the specimen for the injection. In the 11 remaining experiments, 7 of the animals survived the injection and 4 died as a result of it. The total quantities of bile plus pancreatic juice in terms of body weight that were injected in the 4 experi-

ments in which death occurred were 17.5, 15.0, 20.0 and 20.0 cubic centimeters. The corresponding figures for the 7 experiments in which recovery took place were 10.0, 10.0, 10.0, 16.0, 10.0, 15.0 and 20.0 cubic centimeters.

Autopsies on the animals which died showed striking changes. There was a great deal of reddening of all of the peritoneal surfaces and usually an extreme degree of fat necrosis. The fat necrosis in some instances extended above the diaphragm. Free bloody fluid was present in the peritoneal cavity in varying amounts. The small vessels in the peritoneal cavity were definitely dilated.

Although it is a point that is difficult of absolute proof it seemed quite definite that a combination of bile and pancreatic juice exerted more untoward effects than an equal volume of bile or pancreatic juice alone. The action of the combination was undoubtedly greater than that of an equal quantity of pancreatic juice alone.

D. The effects of gastric juice. Nine experiments were performed in which the effects of the injection of gastric juice were studied. The introduction was usually followed by an acceleration of the pulse rate and a change in the appearance of the dog. A slight increase in the concentration of the blood occurred. None of the animals died as a result of the injection of gastric juice. The quantities introduced per kilogram of body weight varied from 7 to 16 cubic centimeters. In 5 of the experiments, the amount was greater than 10 cubic centimeters per kilogram of body weight.

It seemed very definite from these experiments that the injection of gastric juice is less harmful than the introduction of an equal volume of bile alone or a mixture of bile and pancreatic juice.

E. The effects of secretion from the duodenum. Three experiments were performed in which secretion from the duodenum was introduced into the peritoneal cavities of other dogs. There was slight infection present in each instance. None of the recipients died. The quantities introduced per kilogram of body weight were 8.0, 14.0 and 16.0 cubic centimeters.

II. The effects of the injection of the fluids on the cardiac output, blood pressure and ar-

terial inflow Eighteen experiments were performed in which the cardiac output and the maximum and minimum arterial blood pressures were determined before and at varying intervals following the introduction of bile or pancreatic juice or both. A comparison of the studies made at intervals varying from 6 to 30 minutes following the intraperitoneal injection with those performed during the control period shows that both the cardiac output and the maximum blood pressure had declined in 10 of the experiments while a decline in the blood pressure without significant alteration in the cardiac output had taken place in the 8 remaining experiments. It is my belief that the blood pressure declined prior to the drop in cardiac output in all or most of the experiments, but the latter determinations cannot be performed rapidly or repeatedly enough to determine this point. The decline in the minimum pressure which was present in 12 experiments was less than that in the maximum and hence there was a decrease in the pulse pressure. In the 6 remaining experiments, the minimum pressure did not drop.

Further studies were carried out at intervals varying from 40 minutes to 2 hours following the intraperitoneal injection. As compared with the control determinations, there was a decline in the cardiac output and maximum arterial blood pressure in all experiments. The minimum arterial blood pressure was the same as it had been during the control period in 6 experiments, it was slightly higher in 3, and definitely depressed in 9 experiments. A comparison of these determinations performed after an average time of 91 minutes following the intraperitoneal injection with those made shortly after the injection shows that the output of the heart had decreased in 17 of the 18 experiments. The maximum arterial blood pressure had increased in 4 of the experiments, it remained the same in 6 and decreased in 8. The minimum arterial blood pressure increased in 8 of the studies, remained the same in 3, and decreased in 7. The pulse pressure during this period was less than that observed previously.

Although there is some variation in the results of the experiments, in general it can be stated that the most significant early altera-

tion in the circulation following the intraperitoneal injection of bile or pancreatic juice is a decrease in the arterial blood pressure and particularly in the maximum pressure. The output of the heart has usually declined rather greatly an hour or more later without much further alteration in the blood pressure.

An average of the determinations in the 18 experiments gives the following results. During the control period, the cardiac output was 1,356 cubic centimeters per minute, the maximum arterial blood pressure was 163 millimeters mercury, and the minimum blood pressure was 87 millimeters mercury. After an average interval of 14 minutes following the intraperitoneal injection, the average output of the heart was 1,090 cubic centimeters per minute, the maximum blood pressure was 110 millimeters mercury, and the minimum pressure was 75 millimeters mercury. After an average interval of 91 minutes following the injection, the average cardiac output was 688 cubic centimeters per minute, the maximum blood pressure was 100 millimeters mercury, and the minimum pressure was 76 millimeters mercury. The results of a representative experiment are given in Table I.

In some instances the bile or pancreatic juice was infected. The quantity of these fluids that was introduced into the peritoneal cavity in the different experiments varied from 172 to 380 cubic centimeters. The quantity of fluid recovered from the peritoneal cavity at the completion of the experiments varied from 200 to 605 cubic centimeters. The total quantity of bile or pancreatic juice or both that was introduced in all of the experiments was 4,823 cubic centimeters and the total quantity of fluid that was present in the peritoneal cavity at the completion of the studies was 7,715 cubic centimeters. The average quantity injected in cubic centimeters per kilogram of body weight was 20.8 and the average quantity of fluid present later in the peritoneal cavity was 33.3 cubic centimeters per kilogram of body weight. In addition there were small amounts of free fluid in the pleural cavities in some experiments. The duration of these studies varied from 2 to 7 hours, the average duration being 4½ hours. Nine of the animals died and the

remainder were killed painlessly at the end of the observation period.

A fairly wide variation in the arterial inflow rate was observed during the control period and it is my opinion that alterations which were observed subsequently are probably without significance. The femoral arterial inflow rate was determined in 20 experiments. The inflow rate remained approximately the same following the introduction of bile or pancreatic juice or both into the peritoneal cavity in 12 experiments. It increased somewhat in 7 and decreased in 1. The inflow rate as studied in the splenic artery was determined in 9 experiments. There was no definite change in 6 of these and an increase in the 3 remaining. It is to be remembered that an increase in inflow rate indicates a decrease in arterial tone and a decrease in arterial inflow indicates an increase in arterial tone.

#### EVALUATION

When a duodenal ulcer perforates into the free peritoneal cavity there escapes through the opening a mixture of bile, pancreatic juice, gastric juice, duodenal secretion, saliva, and food and liquids, if such are present in the stomach. The quantity of these substances which escapes depends upon the amount of the material present in the stomach at the time, the size of the opening in the duodenum, and the length of time during which it maintains a free communication with the general peritoneal cavity. The amount of infection that is present in the material that escapes into the peritoneal cavity undoubtedly influences to an important extent the chances of recovery of the patient. This was demonstrated conclusively in some of the present experiments in which organisms were introduced intentionally. However the early signs and symptoms appear too rapidly for infection to be a major factor and it is this stage of the process in which we are particularly interested in this paper. It was apparent at the beginning of the studies that many complicating factors would be introduced by making an opening into the duodenum and allowing the secretions to flow into the peritoneal cavity. These would include the anesthetic and the operation, and furthermore one would not be

able to differentiate between the effects of the various types of secretions. It was for these reasons that it was deemed advisable to obtain the secretions from one group of animals and to inject them into a second group.

The experiments which have been described showed very clearly that the introduction of either bile or pancreatic juice or gastric juice or duodenal secretion in large amounts causes signs and symptoms in animals similar to those observed in the human following the perforation of a peptic ulcer. An immediate change in the condition of the animals was observed following the injection; they then seemed to improve for a while and later became quite ill again. Bile seemed to exert more deleterious effects than an equal volume of any one of the other secretions but the most marked changes followed the introduction of a mixture of bile and pancreatic juice. The reason for this is not apparent but it seems possible that the pancreatic juice is activated by the bile, thus increasing the total of the effects.

Horrell (8) has noted that the toxicity of bile varies directly with its salt content and specific gravity and hence that gall bladder bile has a greater toxicity than hepatic duct bile or fistula bile. He (7) found that the injection of bile obtained from the gall bladders of dogs into the peritoneal cavities of other dogs in amounts of 5 cubic centimeters or more per kilogram of body weight caused death within 24 hours. Sterilized bile exerted the same effects.

The initial signs and symptoms that were observed following the intraperitoneal injections appear too early to be explained by the absorption of toxic material. It seems likely that the most important of the early actions of the juices is that of a chemical irritant. This results in a dilatation of the many small intraperitoneal vessels and I believe that it is brought about mainly by direct action on the vessels rather than through nerves, although both methods are probably concerned.

In previous studies (9) it has been shown that secondary shock which is produced by trauma to muscles or the slow withdrawal of blood is associated with first a decline in the output of the heart which is followed later by a decline in the blood pressure. The altera-

TABLE I—EFFECTS OF PANCREATIC JUICE ON THE CIRCULATION

Time	Hemato- crit	Pulse rate per min.	Tempera- ture F	Arterial o <sub>2</sub> vols. %	Venous o <sub>2</sub> vols. %	A V dif. vols. %	Max. B P mm hg	Min B P mm hg	o <sub>2</sub> con- sumption c.c.m. per min	Cardiac output per min c.c.m.	Arterial inflow c.c.m. per min
10 55 a.m. control	36 6	80	98 3	15 84	11 46	4 38	150	92	73 80	1685	10 3
11 45 13 min after injection	41 7	155		16 19	11 52	4 67	101	70	63 84	1367	10 3
1 30 2 hours after injection	47 7	190	99 7	17 62	10 62	7 00	110	89	61 25	875	6 9
2 50	50 4	200		20 20	6 54	13 66	48	42	43 54	319	10 1

Protocol. Experiment 18 8 15 a.m. morphine gr 1 10 55, control determinations. 11 20 to 11 32 285 c.c.m. of infected pancreatic juice introduced into the peritoneal cavity. 11 45 second group of determinations. 2 50 further determinations. 3 45 animal died. Autopsy revealed general reddening of all intraperitoneal structures. There were 430 c.c.m. of blood tinged fluid in the peritoneal cavity and 15 c.c.m. of fluid in each side of the chest.

tions appear in the reverse order when primary shock (2) is produced. In approximately one half of the present experiments, the first determinations following the intraperitoneal injections showed a decrease in both the cardiac output and the blood pressure. In the remaining studies, the early change consisted of a decline in the blood pressure without appreciable alteration in the cardiac output. If methods were available for determining the output of the heart rapidly and repeatedly, I believe that this latter finding would have been observed in most or all of the experiments. At any rate, the alterations in the circulation that occur immediately following the injection of the various secretions appear to be similar to those that are found in primary shock. The studies which were carried out an hour or longer following the injection showed very little change in the blood pressure from that observed immediately after the injection whereas there was a decided decrease in the output of the heart. This phase of the disturbance in the circulatory system is similar to that observed in secondary shock.

My conception of the alterations in the circulation which follow the introduction of these secretions into the peritoneal cavity is as follows. A dilatation of many small vessels is produced by direct contact with the irritating solutions and, to a lesser extent, through nervous agencies. This results in a drop in the blood pressure. After the blood volume decreases as a result of the marked increase in the circulatory bed and the passage of fluid

into the peritoneal cavity, the output of the heart diminishes. The blood pressure is probably prevented temporarily from declining further by vasoconstriction elsewhere.

The escape of fluid from the vessels into the peritoneal cavity is great enough to cause a considerable decrease in the blood volume but not sufficient to account for the entire decline. As to whether or not this quantity added to that which accumulates in the many dilated vessels is sufficient, one cannot state, as there is no accurate method for measuring it.

I have previously attempted a classification (3) of acute circulatory failure from a physiological viewpoint. The various types were classed as hematogenic, neurogenic, vasogenic, and cardiogenic. The condition under consideration does not fall into any single one of these types but is rather a combination of the first three. It is my impression that the early phase is largely vasogenic and the later stage is mainly hematogenic.

#### SUMMARY

Experiments were performed in an effort to find the factors which are responsible in the main for the rapidly developing signs and symptoms that follow the perforation of peptic ulcers. The alterations in the circulation which are produced by the introduction into the peritoneal cavity of the various upper intestinal juices were studied.

Bile, pancreatic juice, gastric juice, and duodenal secretion were obtained by cannulating the various structures. The juices were



injected with a syringe and needle into the peritoneal cavities of other dogs.

The following results were obtained:

1 Following the injection of rather large amounts of one or more of the upper intestinal juices, the animals became ill almost immediately. There was usually an increase in the pulse rate and vomiting.

2 Death did not occur in any of the 9 experiments in which sterile pancreatic juice varying in amounts from 11 to 39 cubic centimeters per kilogram of body weight was injected. Infected pancreatic juice in smaller quantities produced death.

3 Bile that is recovered the first several days following the cannulation of the common duct exerts more ill effects when injected into the peritoneal cavity than that which is collected later. Six experiments were performed in which uninfected bile obtained from animals operated upon less than 4 days previously was injected into other animals in amounts equalling 31 cubic centimeters or less per kilogram of body weight. All of the recipients became quite ill but only 1 died. Bile apparently exerts more untoward effects than an equal quantity of pancreatic juice.

4 Eleven experiments were performed in which equal quantities of uninfected bile and pancreatic juice were injected into the peritoneal cavity. The amounts introduced were closely comparable to those injected in the studies in which bile or pancreatic juice alone was used. Four of the animals died and it seemed quite definite that the combination of bile and pancreatic juice is more toxic than an equal volume of either of them.

5 Death did not occur in any of the 9 experiments in which a corresponding quantity of gastric juice was used or in the 3 experiments in which duodenal secretion was injected. These 2 secretions seemed to result in less harm than a corresponding quantity of bile alone or a combination of bile and pancreatic juice.

6 All of the animals which died as a result of the introduction of one or more of the secretions, exhibited marked reddening of the intraperitoneal structures. This reddening and the presence of massive fat necrosis was par-

ticularly marked in the experiments in which the mixture of bile and pancreatic juice was injected. There was usually a large quantity of free fluid in the peritoneal cavity at autopsy but this quantity by itself alone was not sufficient to account for the decline in blood volume and death. It is possible that this quantity plus the blood that was present in the many dilated intraperitoneal blood vessels might be sufficient. The increase in the concentration of the red blood cells in some experiments was very great while in others it was not marked.

7 Studies on the cardiac output and blood pressure were performed before and following the injection of bile or pancreatic juice or both. Although the results were not identical in all cases the major early alteration consisted of a decline in the blood pressure, as is found in primary shock, and the subsequent change consisted of a greater drop in the cardiac output than in the blood pressure as is found in secondary shock.

BIBLIOGRAPHY

BARTLETT, WILLIAM. An experimental study of the structure in shock. *J. Exper. Med.* 9 2, 3 4 5.  
BLALOCK, ALFRED. Effects of primary shock on cardiac output and blood pressure. *Proc. Soc. Exper. Biol. & Med.* 1933, 3 35.  
1 IDEM. Acute coronary failure as exemplified by shock and hemorrhage. *Burg. Gynec. & Obst.* 1934, 23 55.  
4 KAMAN, ROWEN and McCARTON, J. M. On the collection of the entire external secretion of the pancreas under sterile conditions and the fatal effect of total loss of pancreatic juice. *J. Exper. Med.* 1917, 43 30.  
5 KELLAMER, GERRILL and GAMBER. Studies in secondary traumatic shock. I. The circulation in shock after abdominal injuries. *Ann. J. Physiol.* 1919, 49 90.  
4 HODGINS, JOHN. A Textbook of Surgery p. 247 Springfield: Charles C. Thomas, 1933.  
7 MORGALL, O. R. Experimental bile peritonitis and its treatment in the dog. *Arch. Int. Med.* 1929, 43 84.  
8 IDEM. The toxicity of bile. *Physiological Rev.* 1931, 11 1.  
9 JORDON and BLALOCK. Experimental shock. A study of the effects of hemorrhage, of trauma to muscles, of trauma to the peritoneum, of burns and of histamine on the cardiac output and blood pressure of dogs. *Arch. Surg.* 1931, 1 533.  
EVON, P. and McCLARTY, P. D. A method for the permanent sterile drainage of intra-abdominal fluids, as applied to the common duct. *J. Exper. Med.* 9 2, 37.

## FURTHER QUANTITATIVE DETERMINATIONS OF PROLAN AND ESTRIN IN PREGNANCY

WITH ESPECIAL REFERENCE TO LATE TOXEMIA AND ECLAMPSIA<sup>1</sup>GEORGE VAN S SMITH, M.D., F.A.C.S., AND O. WATKINS SMITH, Ph.D., BROOKLINE, MASSACHUSETTS  
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IN a previous communication (1) we reported the results of quantitative analyses for prolan and estrin in the serum and urine of 42 women during the last third of pregnancy. Ninety-six per cent of the toxemic and eclamptic patients showed excessive amounts of prolan and 69 per cent of them had low levels of estrin—as compared with the figures derived for normal late pregnancy.

The purpose of the present paper is to record additional data on 27 more pregnant women. Six of the patients who showed no toxic symptoms had monthly specimens analyzed throughout pregnancy and the report of monthly analyses on a patient who developed toxemia at the eighth month is reprinted from the previous paper (Table I). The data on 9 additional cases of late pregnancy toxemia, 6 of whom had convulsions, are also given. We have been especially interested in discovering whether or not quantitative analyses for prolan and estrin might be of diagnostic value (1) in differentiating between pre-eclamptic and nephritic toxemia, (2) in predicting the development of toxemia in later pregnancy, (3) as a means of prognosis in patients with clinical signs indicating the beginning of late pregnancy toxemia. Thus far 12 women (besides Cases 1 to 7, Table I), upon whom we have made serum analyses in the middle third of gestation, have been followed clinically to delivery (Table II) with these ideas in view.

The methods of collecting and analyzing specimens have been the same as those described previously (4). The urinary prolan and estrin are expressed in rat units per 24 hour volume and the serum prolan in rat units per 100 cubic centimeters, the figures being based upon the smallest amount of the urine or serum that gave a definitely positive test according to our standards. The limited quantity of blood available made it necessary

to test for estrin each amount of a given serum upon only one or two spayed female rats. The data on serum estrin, therefore, are given in terms of the actual readings, +++ signifying a full estrous smear in one or both rats, ++ a pre-estrous reading, etc.

## QUANTITATIVE ANALYSES THROUGHOUT PREGNANCY—TABLE I

In all 7 of the cases given in Table I, a peak in the level of prolan in serum and urine is noted during the second, third, or fourth month followed by a marked drop. In 5 of the 6 cases who developed no toxic symptoms, the prolan remained low throughout the rest of gestation. The level of estrin in these 5 cases rose as pregnancy advanced, reaching a peak during the last month. Case 7, on the other hand, showed a marked rise in serum prolan during the sixth month accompanied by a drop in urinary estrin. It was nearly 2 months later that the slightest possible trace of albumin appeared in her urine, but by 2 weeks before term, toxemia had become definite (hypertension, edema, and albuminuria) and forced delivery was considered advisable. Because of the findings in this case as compared with normals, we became apprehensive when Case 6 began to show a slight rise in serum prolan and a drop in estrin at 7½ months. At 8½ months the urinary prolan also had increased and the estrin of serum and urine were even lower. This patient, however, had not the slightest evidence of toxemia, had an induced delivery somewhat before due, and a normal puerperium. The apparent contradiction in these 2 cases can perhaps be explained by the fact that Case 6 delivered 1 month after the prolan-estrin imbalance appeared, whereas Case 7 showed her imbalance earlier and developed no toxemia until nearly 2 months afterward. Case 6 was the only normally pregnant woman, both in this group and

<sup>1</sup>The Mrs. William Lowell Putnam Investigation of the toxemias of pregnancy.

TABLE 1—QUANTITATIVE ANALYSES THROUGHOUT PREGNANCY ON 7 WOMEN 6 WITHOUT AND 1 WITH LATE PREGNANCY TOXEMIA

Case Normal. Mrs A R U

[illegible]

Case	Normal	Min	WCB
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		Case	Normal	Min	WCB				
Apr 4: VII part and pregnancy normal. Lungs unclear at first exam. Observed non- coverage by net samples of TBE observed Cats, but not shown by 12 hour 4-11, in dental lab 9-17	1-20-22-24 months occasional intercy changes. Normal	100	1000						100
	3-7-12-4 months occasional intercy changes. Normal	100	700						100
	6-17-22-4 months normal	80	600						100
	6-10-22-4 months normal	20	400			+	+	+	100
	8-15-22-6 months normal	40	600	+	+	+	+	+	100

Case 3 Threatened Miscarriage No toxic symptoms Mrs P O B

[illegible]

Case 4. Threatened Miscarriage Premature delivery at 34 weeks. No toxic symptoms Mrs. S.

Age	Sex	Height	Weight	Build	Complexion	Hair	Eyes	Teeth	Other
1-1-11	M	5-10	140	Medium	Light	Dark	Blue	Good	
1-1-11	F	5-10	120	Medium	Light	Dark	Blue	Good	
1-1-11	M	5-10	140	Medium	Light	Dark	Blue	Good	
1-1-11	F	5-10	120	Medium	Light	Dark	Blue	Good	
1-1-11	M	5-10	140	Medium	Light	Dark	Blue	Good	
1-1-11	F	5-10	120	Medium	Light	Dark	Blue	Good	
1-1-11	M	5-10	140	Medium	Light	Dark	Blue	Good	
1-1-11	F	5-10	120	Medium	Light	Dark	Blue	Good	
1-1-11	M	5-10	140	Medium	Light	Dark	Blue	Good	
1-1-11	F	5-10	120	Medium	Light	Dark	Blue	Good	

TABLE I—QUANTITATIVE ANALYSES THROUGHOUT PREGNANCY ON 7 WOMEN, 6 WITHOUT AND 1 WITH LATE PREGNANCY TOXEMIA—Continued

Case 4 Threatened Miscarriage Premature delivery at 7½ months No toxic symptoms Mrs S—continued

Case History	Date of specimen and clinical condition at time	Prolan		Estrin								Urine
		Serum	Urine	Serum								
		ru per 100 c.cm	ru in 24 <sup>h</sup>	1 c.cm	2 c.cm	3 c.cm	4 c.cm	5 c.cm	6 c.cm	10 c.cm.	ru. in 24 <sup>h</sup>	
Age 32 III para first pregnancy normal sec ond, miscarried at 3 months last catamenia 5 21 33 due 2 25 34 spon taneous de livery 1 13 34	10-10-33-4½ months--normal	40	280					—		+++	1560	
	11-9-33-5½ months--normal	33 3	330			—		+++			1275	
	12-9-33-6½ months--normal	50	700								2400	
	1-9-34-7½ months--	50	530			—		+++			2700	
	1-10-34--ruptured mem branes No mechanical explanation Delivery 1-13-34											

Case 5 Normal. (Mild hypertension when not pregnant) Mrs C P

Age 34 II para first pregnancy 13 yrs. ago sterility for 9 yrs B P 140 when not preg nant last cata menia 9-4-33 due 6-11-34 normal delivery 6-7-34	12-15-33—3½ months—B.P 150 Otherwise normal. Weight 125 lbs	66 6	920							—	230	
	1-12-34—4½ months—B.P 140 Otherwise normal Weight 126 lbs	1000	5900							—	850	
	2-16-34—5½ months—B P 140 Otherwise normal Weight 130 lbs	333	2000			—		+++			1000	
	3-9-34—6 months—B.P 140 Otherwise normal Weight 130 lbs.	100	1150								1900	
	4-6-34—7 months—B P 140 Otherwise normal Weight 137 5 lbs	40	960			—		+++			4000	
	5-15-34—8 months—B.P 142 Otherwise nor mal Weight 145 5 lbs	50	350		+	+++					4000	

Case 6 Normal Mrs A L P

Age 29 III para first two preg nancies 5 and 7 years ago nor mal last cata menia 8-10-33 due 5-17-34 delivered 5-5-34	11-5-33—2½ months—some nausea	200	2040							—	<60	
	12-4-33—3½ months—normal	100	500					—		—	570	
	1-2-34—4½ months—normal	66 6	364					—		—	850	
	2-5-34—5½ months—normal	66 6	400			—		+++			870	
	3-5-34—6½ months—normal	66 6	700	—	+++						5000	
	4-2-34—7½ months—normal	100	700		—	+++					2350	
	4-30-34—8½ months—normal	143	2000			—		+++			1300	

\*Case 7 Toxemia developed during last month Mrs M

Age 33 II para toxemia at 8th month of last pregnancy last catamenia 10-16-32 due 8-2-33 forced delivery due to toxemia 7-22-33	1-12-33—2½ months—vomiting B P 130 Alb o	333	1400					—	±		700	
	2-13-33—3½ months—vomiting B.P 118 Alb o	333	2100					±	+++		760	
	3-16-33—4½ months—well B P 120 Alb o	125	900			±	+++	+++			2700	



This case was included by Cushing (1, Case 5) in his report of hypophyseal changes associated with eclampsia and other hypertensive states. Her pituitary showed the basophilic invasion of the posterior lobe which he considers characteristic. Her serum prolan was the highest we have yet found, i.e., 0.01 cubic centimeter gave a markedly positive Aschheim-Zondek test. In all of the normal pregnancies that we have studied, at 7 months at least 1.0 cubic centimeter of serum was required to give a positive test. Moreover, the estrin content of her serum was low. It is probable that the urinary values are considerably lower than they would have been had the analyses been performed on an earlier specimen, since at the time of collection the kidneys had almost completely shut down. This case well confirms our hypothesis that a marked excess of prolan and a subnormal level of estrin are typical of eclampsia.

CASE 9 Mrs. H. K., aged 40 years, V-para. Previous pregnancies had been normal. Last catamenia was June, 1933. She was admitted to the hospital January 30, 1934, in coma and 7½ months pregnant. A history of convulsions at home was obtained. Three convulsions occurred after admission. Blood pressure was 190/110. The urine contained a heavy trace of albumin. The patient had been well until January 28, when she felt dizzy and noticed that her legs were swollen. Delivery occurred on January 31. The urine was collected for 24 hours after delivery and blood was taken at end of this period. Her blood pressure dropped to normal, eye symptoms disappeared and by February 11 the urine contained only the slightest possible trace of albumin. Clinical diagnosis eclampsia.

Serum prolan 1000 r u per 100 c cm

Urinary prolan 4350 r u in 24 hours

Serum estrin negative with 5 c cm

Urinary estrin 100 r u in 24 hours

Here again the excess of prolan, in spite of the fact that these specimens were collected after delivery, is marked. It is known that the estrin level drops very quickly after delivery (5) and therefore the figures for estrin are probably considerably lower than they would have been a day earlier.

CASE 10 Mrs. M. S., aged 36 years, I-para. Last catamenia was June 25, 1933. Due April 1, 1934. On February 27 the blood pressure was normal, the urine contained a trace of albumin. After 8 days on hospital routine the patient was discharged, there being a slightest possible trace of urinary albumin.

She re-entered on March 28 vomiting and with epigastric pain and headache. Blood pressure was 198/110. Urine contained heavy trace of albumin. She had two convulsions, one before labor was induced on March 28 and one after. Blood was taken at delivery. Clinical diagnosis eclampsia.

Serum prolan 1000 r u per 100 c cm

Serum estrin positive with 3 c cm, negative with 2 c cm

Excessive serum prolan characterized this case, the serum estrin was on the low side of normal.

CASE 11 Mrs. A. K., aged 33 years, VIII-para. All previous pregnancies had been normal. Last catamenia was June 7, 1933. Due March 14, 1934. She was admitted to the hospital March 4, 8½ months pregnant. She had had headaches and scotomas for 3 weeks and epigastric pain for 2 days. One convulsion occurred after entry. Blood pressure was 210/120. The urine contained a heavy trace of albumin with casts. There was generalized edema. Blood was taken immediately after convulsion. Delivery occurred March 5, 1934. Toxemia disappeared. Clinical diagnosis eclampsia.

Serum prolan 200 r u per 100 c cm

Serum estrin positive with 3 c cm, negative with 2 c cm

As has been pointed out (4) the degree of excess of prolan in toxemia does not always run parallel with the severity of symptoms. This patient's prolan, although considerably higher than the normal, was not as high as that of many of the pre-eclamptic cases. It may be that certain women are more sensitive to an endocrine imbalance than others. Another and more likely possibility is that by the time symptoms appear, placental changes may have taken place, with consequent decreased production of prolan and that, if analyses had been made earlier, the excess of prolan would have been more pronounced.

CASE 12 Mrs. M. McD., aged 33 years, VII-para. Previous pregnancies had been normal. The last catamenia was July 4, 1933. She was admitted to the hospital February 27, 1934, 7½ months pregnant. Blood pressure was 140/100. The urine showed trace of albumin with casts. Blood non-protein nitrogen was 72 milligrams per 100 cubic centimeters. The patient had headaches, dizziness, severe pain in right upper quadrant of the abdomen, and an inflamed parotid gland. Premature delivery occurred on February 27. Twelve hours postpartum there were convulsions. Complete anuria ensued. Blood was taken at the time of convulsions.

March 5, 1934 blood non-protein nitrogen, 120, creatinine, 6.5, uric acid, 8.9

TABLE I—QUANTITATIVE ANALYSES THROUGHOUT PREGNANCY ON 7 WOMEN 6 WITHOUT AND 1 WITH LATE PREGNANCY TOXEMIA—Continued

\*Case 7 Toxemia developed during last month. Mrs. M.—continued

Case History	Date of specimen and clinical symptoms at time	Protein		Estrin							
		Serum	Urine	Serum							
				mg per 100 cc	mg per 100 cc	mg per 100 cc	mg per 100 cc	mg per 100 cc	mg per 100 cc	mg per 100 cc	mg per 100 cc
April 25, 11, para, previous 11 full months of last pregnancy last toxemia 10-15-20 Aug 14 (13.6) delivered due to toxemia 21 22	4-1-13—3½ months—well A.H.	pos	neg		+	+++					200
	5-6-13—6½ months—well B.P. 194 A.H.	pos	neg		±	+++					1070
	6-7-13—1 month—well B.P. 194 A.H.	pos	±	—	++	+++					1000
	6-27-13—8 months—well B.P. 194 A.H. E.P.T.	pos	±/neg	±±	+++						3000
	7-2-13—10th ET and edema of ankles										
	7-20-13—10½ months—edema of ankles B.P. 190 and 174 for last 2 weeks		trace								1,200

\*Approved June 24, J. Physiol. 1934, 27: 27. ± T slight trace ±± T slightest possible trace

in the 15 normal cases already reported (4) whose serum prolan after the sixth month was over 100 r.u. per 100 cubic centimeters and it was not until the eighth month that here exceeded this figure. At present we feel that the vital period, in which important information can be derived from quantitative estimations of prolan and estrin, is between the sixth and seventh months and that any marked variation at this time may indicate the development of future complications.

From the data presented in Table I it is apparent that during the early months of pregnancy there are wide individual variations in the quantities of these two hormones. It is thus difficult to relate any particular clinical picture of early gestation to these substances. For example Cases 2, 3, and 4 had miscarried previous pregnancies and threatened to miscarry the pregnancies herein reported. Case 4 had a premature delivery at 7½ months and Case 23 (Table II) had one at 6 months. From the hormone values on these 4 patients, we are unable to associate any endocrine picture with miscarriage. However 5 of the group comprising Table I, Cases 2, 3, 4, 6 and 7 complained of nausea or vomiting during the early months. The low levels of estrin in 4 of

them and the marked rise which accompanied the cessation of these symptoms in all 5 seems more than coincidental. This common complaint usually disappears by the fourth or fifth month at the time when estrin has reached a comparatively high level. The possibility of using this hormone therapeutically remains untried.

#### QUANTITATIVE ANALYSES ON 9 CASES OF LATE PREGNANCY TOXEMIA 6 OF WHOM HAD CONVULSIONS

CASE 8 Mrs. A.Z. aged 31—para. Last toxemia in January 1933. Patient was admitted to the hospital August 1933, in coma, about 7 months pregnant. She had had 40 to 50 convulsions in the previous 24 hours. Her blood pressure was 270. The urine contained a heavy trace of albumin with casts. There was edema of face and ankles. Blood specimen was taken on admission. Urine was obtained by catheter for 4 hours, then complete suppression. She died August 24, 1933. Clinical diagnosis, confirmed by autopsy was eclampsia.

Serum prolan 0.000 r.u. per 100 c.c.m.  
Urinary prolan 0.70 u. in 24-hour volume (calculated from creatinine and patient's weight)  
Serum estrin test negative with 5, 4 and 5 c.c.m.  
Urinary estrin 300 r.u. per 24 hour volume (calculated from creatinine and from the patient's weight)

TABLE II—ANALYSES ON 12 WOMEN IN THE MIDDLE THIRD OF PREGNANCY WHOSE CLINICAL PROGRESS HAS BEEN FOLLOWED TO DELIVERY—Continued

Case History	Date of specimen and clinical condition at time	Follow-up	Prolan		Estrin						
			Serum	Urine	Serum						Urine
			r u per 100 c.cm.	r u. in 24°	1 c.cm	2 c.cm	3 c.cm	4 c.cm	5 c.cm	6 c.cm	r u in 24°
Case 27 Mrs D M Age 33 IV para first pregnancy normal has had toxic symptoms with 2 pregnancies last catamenia 6-16-33 due 3-20-34	1-29-34—7 months— B P 154/112 Alb SPT Edema and dyspnea (First trimester normal)	Toxic symptoms continued throughout pregnancy Normal delivery 3-31-34 4-6-34—SPT alb Clinical diagnosis probably chronic nephritis	335					—		±	
Case 28 Mrs. C P Age 28 IV para, previous pregnancies normal last catamenia 7-20-33 due 4-26-34	1-29-34—6 months— B P 134/95 Alb SPT Headaches dyspnea and edema. Nausea and vomiting for 5 mos	Albuminuria continued and B P increased to 150 Headaches and dizzy spells Delivered 4-29-34 B P and urine normal after delivery Clinical diagnosis toxemia without convulsions	333				±		+++		

S T, slight trace S P T, slightest possible trace

March 14, 1934 blood non-protein nitrogen, 120, creatinine, 3.0, uric acid, 5.6, blood pressure 110/80, urinary albumin, none

Clinical diagnosis acute nephritis, acute parotitis

Serum prolant 66.6 r u per 100 c cm

Serum estrin negative with 5 c cm

This is the second case (the other is Case 28, ref 4) definitely diagnosed as nephritic who has shown a normal low prolant. The low estrin is undoubtedly due to the fact that the blood was collected 12 hours after delivery.

CASE 13 Mrs M G, aged 32, II-para. Toxemia had occurred with last pregnancy. Last catamenia was January 20, 1933. Due October 27, 1933. On September 16 at 7½ months her blood pressure was 140/90. There was no edema or urinary albumin. Blood and urine were collected on September 16.

Serum prolant 200 r u per 100 c cm

Urinary prolant 1300 r u in 24 hours

Serum estrin positive with 3 c cm, negative with 2 c cm.

Urinary estrin 1500 r u in 24 hours

On October 14 she was admitted to the hospital because of toxemia, blood pressure 150/110, slight trace of urinary albumin, and edema of ankles. Delivery occurred on October 16. Blood was taken on October 15. Clinical diagnosis toxemia without convulsions.

Serum prolant 400 r u per 100 c cm

Serum estrin negative with 3 c cm

This patient showed high prolant and low estrin at 7½ months when clinically only

slight hypertension was apparent. A month later, when toxemia was obvious the serum prolant had risen still higher and its estrin had decreased. The figures for this case confirm the evidence presented by Case 7 that in late pregnancy toxemia, the endocrine imbalance is probably present for some time before definite clinical symptoms become manifest.

CASE 14 Mrs A M, aged 37 years, VIII-para. All previous pregnancies had been normal. Last catamenia was May 16, 1933. Due February 22, 1934. Patient had diabetes and was on a diet of 1500 calories without insulin. Blood was taken January 29, 1934, at which time she was 8 months pregnant. She had no nausea, headache, eye symptoms, or edema. Blood pressure was 162/110. The urine showed a slight trace of albumin, three plus sugar. Spontaneous delivery occurred on February 12, 1934. Clinical diagnosis pre-eclamptic toxemia and diabetes.

Serum prolant 333 r u per 100 c cm

Serum estrin positive with 3 c cm, negative with 2 c cm

The high prolant is consistent with the clinical diagnosis of toxemia. Murphy reported high figures for prolant in the urine of the only two diabetics of his series of pregnant women. However, he gave no figures for serum prolant. He did not state the period of gestation when the analyses were made and did not report the progress of the pregnancies. Of Joslin's 89



TABLE II.—ANALYSES ON 12 WOMEN IN THE MIDDLE THIRD OF PREGNANCY WHOSE CLINICAL PROGRESS HAS BEEN FOLLOWED TO DELIVERY

Case History	Date of symptoms and clinical condition at time	Follow up	Pulse		Ecton						
			Systolic	Diastolic	Systolic						Diastolic
					120	120	120	120	120	120	
Case 1. R. Apr. 22, 1900. Last catamenia 3-2-21, due 3-6-21	3-2-21—4 months— normal	No toxic symptoms Normal delivery at term	66 S	44 D	—	—	—	—	—	—	36 D
Case 2. R. Apr. 19, 1902. Last catamenia 3-6-99, due 3-6-99, due	3-2-21—4 months— normal	No toxic symptoms Normal delivery at term	66 S	44 D	—	—	—	—	—	—	36 D
Case 3. M. Apr. 21, 1900. Last catamenia 12-2-21 due 3-6-21, due 3-6-21, due	3-2-21—4 months— normal	Received previous daily throughout pregnancy No toxic symptoms Normal delivery at term	66 S	44 D	—	—	—	—	—	—	36 D
Case 4. M. Apr. 21, 1900. Living child, hemorrhage at term, last catamenia 1-2-21, due 3-6-21, due	3-2-21—4 months— normal	No toxic symptoms Spontaneous delivery 1-2-21 of 5 weeks' premature viable infant	66 S	44 D	—	—	—	—	—	—	36 D
Case 5. M. Apr. 21, 1900. Living child, hemorrhage at term, last catamenia 1-2-21, due 3-6-21, due	3-2-21—4 months— normal	No toxic symptoms Spontaneous delivery 1-2-21 of 5 weeks' premature viable infant	66 S	44 D	—	—	—	—	—	—	36 D
Case 6. M. Apr. 21, 1900. Living child, hemorrhage at term, last catamenia 1-2-21, due 3-6-21, due	3-2-21—4 months— normal	No toxic symptoms Spontaneous delivery 1-2-21 of 5 weeks' premature viable infant	66 S	44 D	—	—	—	—	—	—	36 D
Case 7. M. Apr. 21, 1900. Living child, hemorrhage at term, last catamenia 1-2-21, due 3-6-21, due	3-2-21—4 months— normal	No toxic symptoms Spontaneous delivery 1-2-21 of 5 weeks' premature viable infant	66 S	44 D	—	—	—	—	—	—	36 D
Case 8. M. Apr. 21, 1900. Living child, hemorrhage at term, last catamenia 1-2-21, due 3-6-21, due	3-2-21—4 months— normal	No toxic symptoms Spontaneous delivery 1-2-21 of 5 weeks' premature viable infant	66 S	44 D	—	—	—	—	—	—	36 D
Case 9. M. Apr. 21, 1900. Living child, hemorrhage at term, last catamenia 1-2-21, due 3-6-21, due	3-2-21—4 months— normal	No toxic symptoms Spontaneous delivery 1-2-21 of 5 weeks' premature viable infant	66 S	44 D	—	—	—	—	—	—	36 D
Case 10. M. Apr. 21, 1900. Living child, hemorrhage at term, last catamenia 1-2-21, due 3-6-21, due	3-2-21—4 months— normal	No toxic symptoms Spontaneous delivery 1-2-21 of 5 weeks' premature viable infant	66 S	44 D	—	—	—	—	—	—	36 D
Case 11. M. Apr. 21, 1900. Living child, hemorrhage at term, last catamenia 1-2-21, due 3-6-21, due	3-2-21—4 months— normal	No toxic symptoms Spontaneous delivery 1-2-21 of 5 weeks' premature viable infant	66 S	44 D	—	—	—	—	—	—	36 D
Case 12. M. Apr. 21, 1900. Living child, hemorrhage at term, last catamenia 1-2-21, due 3-6-21, due	3-2-21—4 months— normal	No toxic symptoms Spontaneous delivery 1-2-21 of 5 weeks' premature viable infant	66 S	44 D	—	—	—	—	—	—	36 D

\*The results of analyses on the 1-21 specimens of this patient have been previously reported (A).

TABLE II—ANALYSES ON 12 WOMEN IN THE MIDDLE THIRD OF PREGNANCY WHOSE CLINICAL PROGRESS HAS BEEN FOLLOWED TO DELIVERY—Continued

Case History	Date of specimen and clinical condition at time	Follow up	Prolan		Estrin						
			Serum	Urine	Serum						Urine
					1	2	3	4	5	6	
			r u per 100 c.cm	r u. in 24°	c.cm	c.cm	c.cm	c.cm	c.cm	c.cm	r u. in 24°
Case 27 Mrs. D M Age 33 II para first pregnancy normal has had toxic symptoms with 2 pregnancies last catamenia 6-16-33 due 3-20-34	1-20-34—7 months— B P 154/112 Alb SPT Edema and dyspnea (First trimester normal)	Toxic symptoms continued throughout pregnancy Normal delivery 3-31-34 4-6-34—SPT alb Clinical diagnosis probably chronic nephritis	333					—		± ±	
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The high prolant is consistent with the clinical diagnosis of toxemia. Murphy reported high figures for prolant in the urine of the only two diabetics of his series of pregnant women. However, he gave no figures for serum prolant. He did not state the period of gestation when the analyses were made and did not report the progress of the pregnancies. Of Joslin's 89

diabetic women who were followed in pregnancy 3 developed mild toxemia and one eclampsia. Bowen quoted by Joslin found one probable eclamptic in 10 diabetic pregnancies. Doctor Priscilla White, in a recent personal communication states that among 253 pregnancies in 189 diabetic eclampsia occurred 7 times and toxemia 5 times. These figures represent an incidence of 2.75 per cent of toxemia and of 4.1 per cent of eclampsia in diabetic women. Williams quotes the frequency of eclampsia in the usual run of pregnancy as less than 1 per cent. It would appear that eclampsia is more common in cases of diabetes.

**CASE 5** Mrs. M.F. aged 47 years, 11 para. Previous pregnancies were normal. Last catamenia was November 10, 1933. Due August 7, 1934. Earlier in pregnancy she had had high blood pressure and edema, which had subsided under treatment. She was admitted to the hospital July 26, 1934, with blood pressure of 230/00, a heavy trace of urinary albumin, and 7 pound gain in weight in the last weeks. Eye grounds were negative. Spontaneously she went into labor and delivered a living baby on July 27, 1934. Blood was taken while she was in labor. One month after delivery hypertension, edema and albuminuria had completely disappeared. Clinical diagnosis toxemia without convulsions.

Serum prolactin 200 u. per 100 cc m.

Serum estrin negative with 5 cm.

In this patient the serum prolactin although higher than normal was not as high as would be expected considering the severity of symptoms. The serum estrin however was exceedingly low and as was pointed out in our previous paper (4) a quantitative imbalance between these two hormones may be the significant finding in cases of toxemia.

**CASE 6** E.M.K. aged 7 years, 1 para. She had had no prenatal care. She was admitted to the hospital August 7, 1934, in coma, having had several convulsions. Examination indicated about a 7 months' pregnancy. Blood pressure 220/80. The urine showed large trace of albumin with casts, also ketone. She had 3 convulsions after entry. The uterus as contracting regularly on admission. Blood was taken at delivery. Patient was delivered of macerated fetus August 28 and died August 29.

Blood chemistry August 28 non protein nitrogen, 60 urea, 3.1 unc acid, 7.6 sugar 53.

August 29 non protein nitrogen, 75 urea 4 unc acid, 8.7

*Clinical diagnosis, confirmed by autopsy: eclampsia.*

Serum prolactin 143 u. per 100 cc m.

Serum estrin positive with 5 cm negative with 3 cm.

Again the prolactin and estrin findings in the serum are in keeping with the clinical diagnosis of eclampsia.

In these 9 cases further evidence is found for the assumption that a quantitative endocrine imbalance, due to high levels of prolactin and a tendency toward low estrin, is characteristic of late pregnancy toxemia and eclampsia, that this imbalance is present for some time before symptoms become pronounced (Case 13) and that it is not found in patients whose toxic symptoms are due solely to nephritis (Case 12).

#### ANALYSES IN THE MIDDLE THIRD OF PREGNANCY ON WOMEN WHOSE CLINICAL PROGRESS HAS BEEN FOLLOWED TO DELIVERY (TABLE II)

Of these 12 women 7 (Cases 17-22 and 26) had levels of prolactin within the limits of normal. Clinically Cases 17, 18, 19, and 20 were normal at the time of analysis and throughout the rest of pregnancy except that Case 20 delivered spontaneously 5 weeks before term. Cases 21 and 26 were nephritic and had normal amounts of prolactin. Although she showed some toxic symptoms at the time Case 22 had normal levels of serum prolactin and estrin and her symptoms disappeared soon afterward.

The 5 other women recorded in Table II Cases 23, 24, 25, 27 and 28 all had excessive serum prolactin. Case 23 is the only one of these who showed no toxic symptoms at the time and she delivered 2 days later so that what would have happened had pregnancy continued to term is unknown. Case 24, although having an excess of prolactin at 6 months, as well as an elevated blood pressure and some edema showed normal endocrine values 8 weeks later at which time her toxic symptoms had entirely disappeared. Case 25 had an excess of prolactin at the fifth and sixth months. Her hypertension persisted, but she had no other symptoms except a slight trace of albumin once in the seventh month. In Case 27 we find the first exception to the group diagnosed as nephritic. Her hormones were typical

of pre-eclamptic toxemia in spite of a clinical diagnosis of chronic nephritis. It is possible that both conditions were present. Case 28's high prolant at 6 months associated with the symptoms of toxemia is entirely in keeping with the fact that her symptoms persisted and increased and that the clinical diagnosis was toxemia without convulsions.

In this group, therefore, the finding of normal values for prolant and estrin at around the sixth month was followed in every instance by freedom from the symptoms of pre-eclamptic toxemia throughout the remainder of pregnancy. Of the 3 women with a clinical diagnosis of nephritis, 2 had normal prolant and estrin values, while the other showed high prolant. Of the 5 cases whose prolant was high around the sixth month, all but one had a continuation or increase of toxic symptoms until delivery, and this one showed normal values at 7½ months.

#### SUMMARY

These further quantitative studies of prolant and estrin in 27 additional cases confirm our previous findings of excessive gonad-stimulating hormone and, less consistently, subnormal levels of estrin in the toxemias of late pregnancy and eclampsia. They also indicate that

1 In normal pregnancy a peak in the level of prolant occurs during the second, third, or fourth month, followed by a marked drop. During the remainder of pregnancy the prolant maintains almost a constant level.

2 The amount of estrin increases as pregnancy advances, reaching a peak at term. There is usually a marked elevation of the estrin level between the third and fifth months.

3 In cases of late pregnancy toxemia an excess of prolant has probably been present for some time before the appearance of toxic symptoms. High levels of prolant during the sixth and seventh months in apparently normal women, therefore, may indicate that

toxemia will develop, whereas the finding of normal figures at this time favors the prediction of continued normal pregnancy. A rise after the seventh month may not be significant, since delivery occurs so soon.

4 No abnormal figures for prolant or estrin can be described as typical of miscarriage.

5 The nausea of early pregnancy may be associated with low estrin.

6 Although the highest values for serum prolant yet encountered have been in cases of eclampsia, the degree of excess of prolant does not always run parallel with the severity of the symptoms.

7 Quantitative analyses of serum prolant may be of diagnostic assistance in differentiating between toxemic and nephritic conditions.

8 Quantitative analyses on women who in the middle third of pregnancy are showing some toxic symptoms may be of prognostic value.

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Since this paper was submitted for publication, 12 more pregnant women have been followed from the early months of gestation to delivery. Nine of them were clinically normal throughout and showed typical curves for prolant and estrin. Of the 3 in whom a rise in serum prolant was discovered during the sixth month, 1 had a premature delivery early in the seventh month and the 2 others developed pre-eclamptic toxemia at the eighth month. In 2 of the women who developed no toxic symptoms, the same slight rise in serum prolant as was found in Case 6 (v s) appeared after the seventh month.

#### REFERENCES

- 1 CUSHING, HARVEY. *Am. J. Path.*, 1934, 10, 145.
- 2 JOSLIN, E. P. *The Treatment of Diabetes Mellitus*, p. 869.
- 3 MURPHY, D. P. *Surg., Gynec. & Obst.*, 1933, 56, 914.
- 4 SMITH, G. V., and O. W. SMITH. *Am. J. Physiol.*, 1934, 107, 128.
- 5 SMITH, M. G. *Bull. Johns Hopkins Hosp.*, 1927, 41, 62.
- 6 WILLIAMS, J. W. *Obstetrics*, 1926.

## THE SYNTHESIS OF HIPPURIC ACID

## ITS VALUE IN DETECTING

## HEPATIC DAMAGE SECONDARY TO DISEASES OF THE EXTRAHEPATIC BILIARY SYSTEM

PHILIP F. VACCARO, B.S.; M.D. MONSIEGELA, PENNSYLVANIA

THE determination of hepatic functional efficiency has become a question of paramount importance, particularly in surgery of the biliary tract. Proper interpretation and treatment of certain complications following operative procedures in this region depend upon a comprehensive understanding of the physiological activities of the liver and the extent of their disturbance by hepatic disease. Though much light has been thrown on several aspects of liver function, many more remain obscure. Therefore various complications following operations on the biliary tract still challenge the investigator for a satisfactory explanation.

Recently Dr. William L. Estes, Jr. called our attention to a rather troublesome complication arising in 4 patients following operation for common duct obstruction in his service at St. Luke's Hospital. These patients had recovered favorably from the initial reaction, but on the second or third day the usual post-operative nausea failed to subside. The continued nausea was associated with occasional vomiting, loss of appetite and great weakness. In spite of early treatment with the Jutte tube and other measures, these symptoms persisted for 2 or 3 weeks, leaving the patient in a toxic debilitated condition. 1 of the patients even became drowsy and then semistuporous. None of the operations were technically difficult and aside from a high icteric index and a moderate degree of hepatitis, there was no other indication of hepatic disturbance out of the ordinary. Although all patients were finally relieved, following the administration of glucose intravenously the cause of their symptoms was obscure. It was assumed, however, that noxious substances were being absorbed from the gastro-intestinal tract, with a concomitant impairment of the detoxifying function of the liver.

The urgent desire to solve this problem prompted an investigation of practically all

cases with disease of the biliary tract in this clinic from October 1, 1933 to April 1, 1934. The liver was studied from the aspect of its detoxifying power, the method of Quick being used (16) the synthesis of hippuric acid recently introduced by him as a new test of liver function. The test was utilized not only because it seemed to offer a possible solution for the problem, but also to demonstrate its value in disclosing hepatic damage secondary to diseases of the gall bladder and biliary ducts.

The synthesis of hippuric acid constitutes a detoxifying process brought about by the introduction of benzoic acid into the organism and its subsequent conjugation with glycine. The fate of ingested benzoic acid has been quite extensively studied in man and in various animals, in an effort to explain the chemical changes involved and the site of synthesis of hippuric acid. Benzoic acid ingested by man is combined with glycine and eliminated in the urine almost completely as hippuric acid, except, perhaps, for a small portion which may be combined with glycuronic acid and eliminated as glycuronic acid monobenzoate (12).

Though Lachner, Levinson, and Morse first suggested that hepatic disease disturbs the synthesis of hippuric acid, little attempt had been made prior to the work of Quick (13, 16) to apply the synthesis for the detection of hepatic damage in man. The only previous work showing a reduction in the output of hippuric acid in man with hepatic involvement was that of Bryan. The earlier work of Bunge and Schmiedeberg rather conclusively established that in the dog the synthesis occurs only in the kidney. Quick (13) has recently confirmed the original work of Bunge and Schmiedeberg in the dog, but in the rabbit he found, as did Friedmann and Tachau, that the liver partakes in the synthesis. He believes that in man, as in the rabbit, the syn-

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thesis also occurs in the liver(16) Quick(12) has shown that the organism has no store of preformed glycine and the rate of synthesis of hippuric acid is governed by the ability of the organism to produce glycine. Also, the organism has a definite maximum capacity to produce this substance, for regardless of the amount of benzoic acid taken in, the hourly output of hippuric acid (in the absence of exogenous glycine) remains relatively constant. Since glycine is generally considered to be synthesized in the liver, it was thought that certain types of liver damage might disturb the synthesis and result in a diminished output of hippuric acid.

The present investigation on the excretion of hippuric acid was in a group of 44 cases. Although primarily concerned with liver damage secondary to diseases of the extra-hepatic biliary system, our interest spread so that a few cases with other pathological involvement of the liver were also studied. Ten subjects, clinically free of hepatic and renal disease, were used as control cases to establish the normal output of hippuric acid. Twenty-seven cases had diseases of the gall bladder and bile passages, of which 26 were inflammatory and 1 was carcinoma. All cases, excepting one of catarrhal jaundice, came to operation or autopsy. The excretion of hippuric acid was compared with the gross pathological findings and, when possible, with other liver function tests of more established significance. There were also 3 cases of carcinoma, 3 of cirrhosis, and 1 of chronic passive congestion of the liver. Two of the 3 cases of carcinoma were discovered at operation and the test was run subsequently to determine the rate of excretion of hippuric acid and to compare the result with the bromsulphalein test.

The technique followed was identical with that outlined by Quick (15-16) in his "Simple Clinical Method" as follows:

Five and nine tenths grams of sodium benzoate dissolved in 30 cubic centimeters of water is administered 1 hour after breakfast consisting of coffee and toast. The patient is then given a half glass of water. Immediately after taking the drug the patient voids, and then collects complete hourly specimens for 4 hours. These are preserved with toluene, and hippuric acid determined in each

TABLE I—EXCRETION OF HIPPURIC ACID IN NORMAL SUBJECTS\*

Subject	1 hour	2 hour	3 hour	4 hour	Total
1	0.63	0.98	0.78	0.77	3.16
2	0.60	0.92	1.07	0.75	3.34
3	0.54	0.87	1.01	0.64	3.06
4	0.82	1.01	1.10	0.43	3.46
5	0.77	1.05	0.96	0.76	3.54
6	0.82	1.05	0.99	0.42	3.8
7	0.38	0.61	1.13	0.86	2.98
8	0.41	1.02	0.73	0.87	3.03
9	0.51	0.69	0.97	1.02	3.19
10	0.44	0.93	1.08	0.68	3.13

\*Hippuric acid in terms of benzoic acid in grams

specimen. Each hour specimen is measured, transferred to a small beaker and acidified with concentrated hydrochloric acid until acid to congo red, 1 cubic centimeter of the acid is usually sufficient. The solution is vigorously stirred until the precipitation of hippuric acid is complete, and then is allowed to stand for 1 hour at room temperature. The precipitate is filtered off on a small Buchner filter plate, washed with a small quantity of cold water, and allowed to air dry. The hippuric acid thus obtained is either weighed (to the second decimal place, which is usually sufficient) or titrated with two-tenths normal sodium hydroxide, phenolphthalein being used as indicator. To obtain the total hippuric acid one must add to the amount thus obtained the calculated quantity remaining in solution, 100 cubic centimeters of urine will dissolve 0.33 gram of hippuric acid. In case a specimen exceeds 125 cubic centimeters it should be slightly acidified with acetic acid and concentrated on the water bath to about 50 cubic centimeters before precipitating the hippuric acid. The results are best expressed in terms of benzoic acid. To convert hippuric acid to benzoic, one multiplies by 0.68. In normal adults the output of benzoic acid as hippuric acid is approximately 1 gram or more during the second and third hours and the total for 4 hours is from 3 to 3.5 grams.

Two cases were given glycine, to observe the effect of this substance on reduced hippuric acid excretion in hepatic disease. Five grains, three times a day, was administered 2 days before repeating the test.

The results obtained in this investigation show that the excretion of hippuric acid rather consistently bears out the condition of the liver. The excretion in the 10 control cases was 1 or more grams for the second and third hours and ranged from 2.98 grams to

TABLE II—EXCRETION OF HIPPURIC ACID IN DISEASES OF THE BILIARY TRACT

Case and age	Duration of symptoms	Sclerotic nodules	Vanishing direct indirect—negative reactions per cent of total	Bromsulphalein per cent of dye retained after 20 minutes	Hippuric acid in tenths of gramme					Diagnosis, pathological findings, result
					hr	hr	hr	hr	Total	
J.A.	77½		Direct delayed positive indirect		65	30	25	54	174	Chronic cholecystitis. Liver appeared normal. Unsuccessful recovery.
S.L. 45	77½			10% after 10 min. 15% after 20 min.	43	30	30	8	111	Chronic cholecystitis with lithosis. Liver appeared normal. Unsuccessful recovery.
E.B. 53	77½				70	30	30	34		Chronic cholecystitis. Liver appeared normal. Unsuccessful recovery.
A.T. 44	77½	6			60	51	41	4		Chronic cholecystitis. Liver appeared normal. Unsuccessful recovery.
J.B. 59	77½	6			77	73	36	76	262	Chronic cholecystitis. Liver appeared normal. Unsuccessful recovery.
J.M. 29				17% after 10 min. 26% after 20 min.	46	36	46	46	174	Chronic cholecystitis with lithosis. Liver appeared normal. Unsuccessful recovery.
J.B. 57	77½			17% after 10 min. 26% after 20 min.	51	47	30	6		Chronic cholecystitis with lithosis. Liver appeared normal. Unsuccessful recovery.
S.F. 44	77½		Direct delayed negative indirect		71	83		46		Acute cholecystitis. Liver appeared normal. Unsuccessful recovery.
M.M.	77½				46		52	46	144	Chronic cholecystitis with lithosis. Common duct dilatation. 1½ inch wide. Marked hepatomegaly and steatorrhea. Unsuccessful recovery.
O.A. 43	77½				41	29	36	41 41 41	127 127 127	Chronic cholecystitis with lithosis. Half of gall bladder present. Choleliths. Marked hepatomegaly and steatorrhea. Unsuccessful recovery.
M.L. 44	66½	10		10% after 10 min. 15% after 20 min.	46			51	97	Chronic cholecystitis. Liver appeared normal. Gall bladder enlarged. Marked steatorrhea. Spleen markedly enlarged. Unsuccessful recovery.
C.A. 26	77					51	71	46	168	Chronic cholecystitis with lithosis. Marked hepatomegaly and steatorrhea. Unsuccessful recovery.
J.M. 77					46	46	46	30 46	168 168	Chronic cholecystitis. Marked hepatomegaly and steatorrhea. Unsuccessful recovery.
J.D. 43	77½				17	36		36	111	Chronic cholecystitis with lithosis. Liver enlarged. Gall bladder perforated, markedly thickened and gangrenous. Marked steatorrhea and hemolysis. Unsuccessful recovery.
M.L. 33	77					41	36	30	107	Chronic cholecystitis with lithosis. Moderate amount of hepatomegaly and steatorrhea. Unsuccessful recovery.
M.E. 44	66½		Direct immediate positive indirect		46	31	31	36	144	Chronic cholecystitis with lithosis. Liver enlarged with considerable steatorrhea. Unsuccessful recovery.
S.B. 35	66½				46	77	36	46	168	Chronic cholecystitis with lithosis. Liver slightly enlarged. Mild hepatomegaly. Unsuccessful recovery.
S.B. 77	20		Indirect	negative	41	41	41		127	Chronic cholecystitis with lithosis. Steatorrhea common and hemolysis. Marked hepatomegaly and steatorrhea. Unsuccessful recovery.
J.E. 44	77½				46	30	46	51	174	Chronic cholecystitis with lithosis. Mild hepatomegaly, otherwise liver appeared normal. Steatorrhea in common duct. Unsuccessful recovery.

\*By color determination.

†In 10 weeks after operation, standard technique.

TABLE II.—EXCRETION OF HIPPURIC ACID IN DISEASES OF THE BILIARY TRACT—Continued

Case and age	Duration of symptoms	Icteric index	Vandenberg direct indirect—mgm bilirubin per 100 c.cm of blood	Bromsulphalein per cent of dye remaining after injection	Hippuric acid in terms of benzoic acid in grams					Diagnosis pathological findings result
					1 hr	2 hr	3 hr	4 hr	Total	
20 J R 43	4 yrs.	5		70% after 30 min 10% after 60 min	0.08 0.15	0.07 0.18	0.33 0.46	0.50 0.34	1.03 1.3	Chronic cholecystitis with lithiasis Marked hepatitis and fibrosis Stormy convalescence
21 E Y 33	3 yrs	60	Direct immediately positive indirect 10.0 mgm		0.40	0.81 (1.0-9.33)	0.86 (1.0-9.33)	0.64	2.80	Acute exacerbation of chronic cholecystitis and lithiasis Stone in common duct. Liver palpable (Clinical diagnosis)
21 E Y 33	3 yrs	2	Direct delayed positive indirect 0.2 mgm		0.31	0.63 (2.18-3.4)	0.89 (2.18-3.4)	0.92	2.75	Chronic cholecystitis with lithiasis Stone in common duct. Gall bladder greatly thickened. White bile Cholangitis. Extensive hepatitis and fibrosis. A large number of stones had eroded through the anterior wall of the gall bladder and had become encapsulated in the substance of the liver. Uneventful recovery
22 E S 70	3 mos	50			0.20	0.14	0.09	0.09	0.52	Carcinoma of the gall bladder with metastasis to the liver (Autopsy)
23 S C 56	1 yr	4			0.22	0.05	0.89	0.58	2.64	Chronic cholecystitis with lithiasis Liver slightly enlarged. Moderate amount of fibrosis. Uneventful recovery
24 M S 56	1 yr	12		60% after 30 min	0.44	1.03	0.23	0.49	3.19	Chronic cholecystitis with lithiasis. Slight hepatitis otherwise liver appeared normal. Uneventful recovery
25 J D 35	8 yrs	3	Direct delayed positive indirect 0.8 mgm		0.82	0.87	1.10	0.31	3.10	Chronic cholecystitis with lithiasis. Stones in common and hepatic ducts. Marked hepatitis and fibrosis. Died 23 days after operation from cardiac decompensation
26 H S 20		20	Direct immediately positive indirect 1.5 mgm		0.34	0.51	0.40	0.42	1.67	Catarrhal jaundice (Clinical diagnosis)
27 A F 40					0.85	0.99	0.79	0.48	3.11	Cholecystectomy 1 year ago—(2-1-33) (Chronic cholecystitis with lithiasis mild fibrosis) Admitted for pain in epigastrium 3-5-34 Discharged improved

Clycine administered

†Two weeks after operation standard technique

3.54 grams for the total of 4 hours. Table I confirms Quick's (16) findings as the normal output for adults.

The excretion of hippuric acid was found to be within normal limits in biliary tract disease where the liver appeared normal (Table II, Cases 1 to 8, inclusive). A definite inhibition was noted in practically all cases presenting gross structural changes of the liver (Cases 9 to 23 inclusive). Generally, the degree of inhibition corresponded to the amount of hepatic damage. The only exception was in Case 25, which produced a normal output in the presence of marked structural change of the liver, and in Case 24 with only a slight involvement. The bromsulphalein test in

Case 24, however, was out of proportion to the amount of apparent hepatic damage. A uniformly lowered output was observed in biliary obstruction, Cases 9, 11, 16, 18, 21 and 22. Case 22, with obstruction due to gall bladder carcinoma, yielded the low result of 0.52 gram benzoic acid as hippuric acid excreted in 4 hours. Case 21 illustrates Quick's (16) observation, that the clearance of jaundice does not necessarily mean the liver has returned to normal. The patient at the height of jaundice excreted 2.80 grams benzoic acid as hippuric acid while 4 months later after complete disappearance of jaundice the excretion was 2.75 grams. Case 26 of catarrhal jaundice registered a decidedly low output



TABLE III—EXCRETION OF HIPPURIC ACID IN CARCINOMA, CIRRHOSIS, AND CHRONIC PASSIVE CONGESTION OF THE LIVER

Case and age	Duration of symptoms	Laboratory studies	Bromsulphalein per cent of dye excreted after injection	Hippuric acid in terms of benzoic acid in grams					Diagnosis, pathological findings, result
				1 hr	2 hr	3 hr	4 hr	Total	
A. K. 45	6 mos.		90% after 30 min.		44	87	76	207	Acetophenanthrene Discharged improved (Clinical diagnosis)
J. C. 50	10 mos.			1.5	16	54	23	24	Carcinoma of the liver with metastases. Discharged improved (Clinical diagnosis)
L. S. 37	7 yr.		90% after 30 min.		36	53	45	134	Chronic passive congestion. Liver markedly enlarged (Clinical diagnosis)
L. S. 38			90% after 30 min. after 1 hr.	90	23	84	94	291	Carcinoma of liver (autopsy). Liver unenlarged, largest and surface studded with carcinoma nodules. Uncovered occasionally while exploring the abdomen during the repair of large subdiaphragmatic hernia.
M. M. 50	3 yr.		90% after 30 min. after 1 hr.	91	54	44	52	241	Carcinoma of liver (autopsy). Liver carcinoma of acinar type. Liver slightly enlarged, entire surface studded with secondary nodules. (Diagnosis laboratory). Per minute collection.
M. C. 50	10 mos.			29	24	43	51	147	Carcinoma of liver (autopsy). Liver palpable, large nodular mass in appearance corresponding with left lobe of liver as patient with extensive carcinoma of right breast with metastasis to axilla. (Diagnosis of liver involvement clinical)
C. K. 49	10 mos. ?		48% after 30 min.	4.3		7	86	97	Hypertrophic cirrhosis (Clinical diagnosis)

Except in Cases 24 and 25 the hippuric acid test seemed to be more accurate than the bromsulphalein test in foretelling the condition of the liver.

A diminished excretion also resulted in carcinoma, cirrhosis and chronic passive congestion of the liver (Table III). The bromsulphalein test also indicated extensive damage in this last group of cases.

The second line of figures in Cases 10 and 20, Table II, indicates that the excretion of hippuric acid depressed by hepatic disease is slightly but definitely increased following the administration of glycine. The excretion again diminished when glycine was withdrawn, as shown by the third line of figures in Case 10.

#### EVALUATION

The test is contra indicated in nephritis with nitrogen retention, because the behavior of hippuric acid is not unlike other nitrogenous excretory products. (6) Another disadvantage is that the sodium benzoate is sometimes vomited. Three cases were encountered in this study that could not be subjected to the test because the sodium benzoate was repeatedly vomited.

The manifold duties of the liver with its remarkable power of regeneration and func-

tional reserve, constitute a great obstacle in the accurate determination of hepatic efficiency. However as pointed out by Quick (16) "It must not be forgotten that various functions of the liver are not distinct and independent, but closely interrelated, so that an injury to one may affect several others as well. Certain mechanisms of the liver are so delicate, that there is practically no margin of safety.

Glycine is not only involved in the detoxication of benzoic acid but also a supply is necessary in the synthesis of glycocholic acid (8). Glycocholic acid, most prominent bile acid in human bile is formed by the union of cholic acid with glycine. It is reasonable to assume therefore that the mechanism effecting the conjugation of benzoic acid with glycine, to form hippuric acid and the one affecting the conjugation of cholic acid with glycine to form glycocholic acid are similar. The latter being a normal physiological process, perhaps, utilized incidentally to rid the body of a noxious substance. The synthesis of glycine seems to have little reserve for the diminished excretion of hippuric acid in catarrhal jaundice is out of proportion to the amount of hepatic damage (15, 16). Also Smyth and Whipple, found that a dose of

chloroform insufficient to produce any demonstrable change in the liver cells, caused a definite decrease in the excretion of bile acids. This related functional disturbance may again be demonstrated clinically. Green, Walters, and Frederickson have shown that in biliary obstruction, the formation of bile acids is greatly depressed. The same condition in the present investigation shows in agreement with both Bryan and Quick, a diminished output of hippuric acid.

The influence of benzoic acid and glycine on the excretion of uric acid is interesting. Lewis and Karr were first to observe that the ingestion of benzoic acid decidedly depressed the excretion of uric acid. This finding was confirmed by Swanson, who found that there was not only a marked decrease in the uric acid content of the urine but also an increase in the uric acid content of the whole blood and plasma. The ingestion of glycine on the other hand, according to Lewis, Dunn, and Doisy, more recently to Christmann and Mosier, is followed by an increased excretion of uric acid. Quick (12, 14) finds also that glycine "like other glycogenetic amino acids not only stimulates the excretion of uric acid but also prevents and counteracts the depressing action of benzoic acid." Bruhl doing microscopic studies on the glomerular circulation in the frog found that the circulation stops when there is a lack of glycine. Watzdse previously had made similar observations. In the light of these observations, it seems that glycine has a definite stimulating action on kidney function.

It would seem probable, therefore, that hepatic damage disturbing the synthesis of glycine may exert a depressing action on kidney function. On this basis might be explained the type of "liver death" which has been cited by Heyd with manifestations of renal involvement.

#### SUMMARY AND CONCLUSION

The results obtained in the present study show

1 The excretion of hippuric acid in normal subjects was one or more grams for the second and third hours and a total of 2.95 to 3.54 grams for 4 hours.

2 The excretion was diminished in diseases of the extrahepatic biliary system, presenting gross structural changes of the liver. Obstructive jaundice registered a uniformly lowered output. Generally, the inhibition was governed by the amount of damage.

3 Hepatic damage from carcinoma, cirrhosis, and chronic passive congestion also gave a reduced output.

4 Excretion of hippuric acid reduced as a result of hepatic disease was slightly increased by the administration of glycine.

5 A similar complication alluded to previously was not encountered though two cases, 10 and 20 Table II, with mild manifestations and of shorter duration, had a decidedly low output.

From these observations it is concluded that the hippuric acid test is a method of considerable merit not only to disclose but also to give an approximate amount of structural hepatic damage resulting from diseases of the biliary tract. It also is of value in detecting hepatic damage from other pathological involvement of the liver.

#### BIBLIOGRAPHY

- 1 BRUHL, H. Quoted by A. J. Quick (14). *Arch ges Physiol*, 1928, 220, 380.
- 2 BRYAN, A. W. The value of the sodium benzoate test of renal function, and the effect of injury of the liver on hippuric acid synthesis. *J Clin Invest.*, 1925, 2, 1-33.
- 3 BUNGE, G., and SCHMEIDEBERG, O. Ueber die Bildung der Hippursäure. *Arch f exper Path u Pharma kol*, 1877, 6, 233-255.
- 4 CHRISTMANN, A. A., and MOSIER, E. C. Purine metabolism. II. The effects of the ingestion of glycine on the excretion of endogenous uric acid. *J Biol Chem*, 1929, 83, 11-19.
- 5 FRIEDMAN, E., and TACHAU, H. Ueber die Bildung der Glykokolle in Tierkörper. I. Synthese der Hippursäure in der Kaninchenleber. *Biochem Ztschr*, 1911, 35, 68-103.
- 6 GREEN, C. H., WALTERS, W., and FREDERICKSON, C. H. The composition of the bile following relief of biliary obstruction. *J Clin Invest.*, 1930-1931, 9, 295-310.
- 7 HEYD, C. G. Liver function and liver deaths. *Surg Gynec & Obst*, 1933, 57, 408.
- 8 HOWELL, Text Book of Physiology, 10th ed, pp 830 and 872. Philadelphia, W. B. Saunders Co.
- 9 LACHNER, E., LEVINTON, A., and MORSE, W. Aspects of hippuric acid conjugation. *J Biol Chem*, 1915, 33, 16-18.
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Case and age	Duration of symptoms	Icteric index	Bromsulphalein per cent of 45 remaining after 15 minutes	Hippuric acid in terms of benzoic acid in grams					Diagnosis, pathological findings, result
				1st	2d	3d	4d	Total	
A. K. 45	none		60% after 30 min	27	43	67	70	207	Atrophic cirrhosis. Discharged improved. (Clinical diagnosis)
J. C. 36	6 mos			13	30	64	24	131	Cirrhosis of the liver with ascites. Discharged improved. (Clinical diagnosis)
L. B. 27	37		30% after 30 min		30	53		83	Chronic passive congestion. Liver markedly enlarged. (Clinical diagnosis)
L. B. 36			30% after 30 min after 60 min	70	54	34	34	192	Carcinoma of liver (metastatic?). Liver somewhat enlarged and surface studded with numerous nodules. Observed accidentally while exploring the abdomen during the repair of a large umbilical hernia.
V. M. 36	3 yrs		30% after 30 min after 60 min	47	60	64	37	208	Carcinoma of liver (metastatic) from carcinoma of sigmoid. Liver markedly enlarged, surface on face studded with numerous nodules. (Diagnosis laparotomy?) Per marked edema.
M. C. 60	none			70	34	47	54	185	Carcinoma of liver (metastatic?). Liver palpably large nodules noted in quadrants corresponding with left lobe of liver in patients with carcinoma of right breast with metastases to axilla. (Diagnosis of liver metastases absent.)
C. B. 41	none?		67% after 30 min			77	66	143	Hypertrophic cirrhosis. (Clinical diagnosis)

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#### BIBLIOGRAPHY

1. BRUHL, H. Quoted by A. J. Quick (14). *Arch. ges. Physiol.* 1928, 220, 389.
2. BRYAN, A. W. The value of the sodium benzoate test of renal function and the effect of injury of the liver on hippuric acid synthesis. *J. Clin. Invest.* 1925, 2, 1-33.
3. BUNGE, G., and SCHMEIDEBERG, O. Ueber die Bildung der Hippursäure. *Arch. f. exper. Path. u. Pharmacol.* 1877, 6, 233-255.
4. CHRISTMANN, A. A., and MOSIER, E. C. Purine metabolism. II. The effects of the ingestion of glycine on the excretion of endogenous uric acid. *J. Biol. Chem.*, 1929, 83, 11-19.
5. FRIEDMANN, E., and TACHAU, H. Ueber die Bildung der Glykokolls in Tierkörper. I. Synthese der Hippursäure in der Kaninchenleber. *Biochem. Ztschr.* 1911, 35, 68-103.
6. GREEN, C. H., WALTERS, W., and FREDERICKSON, C. H. The composition of the bile following relief of biliary obstruction. *J. Clin. Invest.*, 1930-1931, 9, 295-310.
7. HEYD, C. G. Liver function and "liver deaths." *Surg. Gynec. & Obst.* 1933, 57, 408.
8. HOWELL. *Text Book of Physiology*, 10th ed., pp. 830 and 872. Philadelphia: W. B. Saunders Co.
9. LACHNER, E., LEVINSKY, A., and MORSE, W. Aspects of hippuric acid conjugation. *J. Biol. Chem.* 1918, 33, 16-18.
10. LEWIS, H. B., and KARR, W. G. Studies in the synthesis of hippuric acid in the animal organism. III. Excretion of uric acid in man after ingestion of sodium benzoate. *J. Biol. Chem.*, 1916, 25, 13.

- LEWIS, H. B. Dr. M. S. and DORR, E. A. Studies in uric acid metabolism. II. Proteins and amino acids as factors in stimulation of endogenous uric acid metabolism. *J. Biol. Chem.* 1917, 26, 9-20.
- QUICK, A. J. The composition of benzoic acid in man. *J. Biol. Chem.* 21, 93-95.
5. Idem. The site of the synthesis of hippuric acid and phenylacetic acid in the dog. *J. Biol. Chem.* 21, 95-113.
6. Idem. The relation between chemical structure and physiological response. III. Factors influencing the excretion of uric acid. *J. Biol. Chem.* 23, 57-69.
7. Idem. Conjugation of benzoic acid with glycine: test of liver function. *Proc. Soc. Exper. Biol. & Med.* 1917, 20, 101-105.
8. Idem. The synthesis of hippuric acid: new test of liver function. *Am. J. M. Sc.* 1917, 71, 670.
9. SARTER, F. S. and WATKINS, G. H. Quoted by A. J. Quick (10). *J. Biol. Chem.* 22, 59-63.
10. SARTER, F. S. and WATKINS, G. H. The effect of sodium benzoate ingestion upon the composition of the blood and urine with especial reference to the synthesis of glycine in the body. *J. Biol. Chem.* 1917-1918, 22, 565-573.
11. THIRAKAK, G. Quoted by A. J. Quick (10). *Arch. ges. Physiol.* 1917, 19, 604.

## DYSOCTOGENETIC AND MIXED TUMORS OF THE UROGENITAL REGION

WITH A REPORT OF A NEW CASE OF SARCOMA BOTRYOIDES VAGINAE IN A CHILD, AND COMMENTS UPON THE PROBABLE NATURE OF SARCOMA

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**I**N 1908 a case of infantile vaginal botryoid tumor came under observation and so interested me on account of its peculiar appearance, rapidly fatal course, and evident rarity that I reported it.

Some ten years later in conversation with Dr. Joshua L. Sackett I mentioned the case and suggested that it probably had its origin in a defect of embryonal development when to my surprise he remarked that he was sure it had and that although I had discovered no evidence of the fact it was really a mixed tumor belonging to the same class as those about which he had written his Inaugural Dissertation for the degree of Doctor of Medicine at the University of Wisconsin in 1901. I was embarrassed to think that I had overlooked his dissertation but when he later kindly presented me with a copy I understood why. My literary research had been concentrated upon the subject of sarcoma and his paper was entitled *Die Mischgeschwülste am unteren Ende des Urogenitalapparates der Kinder*. Ten more years were to pass before opportunity to review the subject afforded in the form of a specimen and case report sent by Dr. A. L. Combs of the Nichol-

son Senn Hospital in Omaha, Nebraska, with permission to publish the case if it proved to be sufficiently interesting. The following is the protocol.

A little girl 6 years of age came to the hospital, January 5, 1932, with a small cystic polypoid tumor mass growing from the anterior wall of the vagina and projecting from the vulva. It was excised, and a treatment of 600 milligrams hours of radium administered. But in about months the patient was back again, with a recurrence covering about 1 1/2 inches of the right wall of the vagina, and made up of aggregation of small cyst like masses. These were also excised, the bases cauterized, and a treatment of 200 milligrams hours of radium applied by inserting the agent deeply into the tissues. This also failed and in January 23, 1933, when the patient was again seen, a large recurrent mass almost completely filled the vagina. As the repeated excisions, supplemented by the use of radium, had failed, further treatment was not urged, although the tumor seemed to be localized in the vagina, the finger in the rectum failing to find anything in the pelvis.

From this time on the patient's condition became steadily worse and the attending physician describes what subsequently happened as follows:

The vaginal mass distended the vulva opening that seemed to be the extreme limit, causing pressure necrosis of the skin margin, which became

covered with heavy crusts. The urethral orifice disappeared from view, the urine escaping between the lobes of the tumor. There was, however, no considerable retention, the patient always being able to void the urine. The external portion of the tumor seemed to break down, diminishing in size and becoming covered with a heavy crust, the internal portion, which was easily palpated, extended to about an inch below the umbilicus and some 2.5 inches to the left. The pelvic pressure seemed to cause contractures of the legs that were tightly drawn up upon the abdomen. The rectum seemed to have perforated about 4 weeks before death, which took place on November 15, 1932.

The necropsy was performed at the home of the patient, in a small town in Nebraska, by the family physician, who was kind enough to furnish the following details:

The pelvis was eviscerated, the tumor, the rectum, the uterus, the vagina, and the ovaries being removed in one large partly amalgamated mass. Casual examination of the liver, kidneys, spleen, and vermiform appendix, revealed nothing abnormal. The thorax and cranium were not opened.

The removed mass of pelvic contents was placed in a jar of formaldehyde and later forwarded to me. It is unfortunate that the tissues could not have been more carefully examined in the fresh condition, as the formaldehyde not only firmly fixed them in a position of considerable distortion, but also rendered them very brittle. This is what I found:

The general tissue mass measures 15 by 10 centimeters, and consists principally of neoplastic tissue, whose lower part, about as large as a good sized orange, lobulated, incrustated, necrotic, and made up of alternating soft and firm substance, is probably that which protruded through the vulvar orifice during life (Fig. 1). Except for a short and narrow strip of wrinkled skin, supposed to be from one of the labia, nothing can be definitely identified as belonging to the external genitalia. The evisceration was evidently performed through the abdominal opening, and the attachments cut away from the inside. Most of the urethra has become amalgamated with the tumor mass, and the meatus has been lost through ulceration. About 8 centimeters of compressed rectum is loosely attached to the left side of the mass, through which its lower part passes to open in a deep fissure on its inferior posterior surface.

The presence of a small quantity of fecal matter throughout its whole length shows that, although compressed into a flattened ribbon, the rectum was patulous, and the suspected rupture had not occurred. Except for a very limited extent in the immediate neighborhood of the anus the rectum

escaped invasion by the tumor. The vagina is so altered as to be scarcely recognizable. It is 7 centimeters in length and 6 centimeters in width and when divided longitudinally (Fig. 2), is found to contain a large irregular space with surrounding walls which vary from one-half to 2 centimeters in thickness. The tissue of these thickened walls must have been very soft and necrotic, but after fixation in the formaldehyde, crumbles away, leaving a curious appearance resembling a tangled mass of pale colored slender worms—probably thrombosed blood vessels.

The uterus, broad ligaments, and ovaries (Fig. 3) are pushed up and to the left, the body of the uterus being ante flexed and its anterior surface adherent to the bladder.

There are a number of flattened neoplastic discs in the broad ligament of the right side, and on the peritoneal surface of the uterus and both ovaries, representing lymphatic metastasis or local extension of the tumor by permeation. Whether there may have been metastasis to the lungs, can never be known as the necropsy did not include the opening of the thoracic cavity.

The upper anterior vaginal wall is completely amalgamated with the neck and posterior wall of the bladder to form a tumor mass 4 centimeters in thickness, projecting into the bladder from behind, and almost completely filling it (Fig. 2). Faint striations, caused by the survival of some of the normal structures in the midst of the general neoplastic mass, indicate the original limits of the bladder and vagina.

Some well preserved parts of the tumor present a finely fasciculated appearance, others are homogeneous. The color, changed by fixation, is pale grayish yellow, and the consistence is firm, though the impression cannot be escaped that it was originally very soft, and probably edematous. But it is neither cystic nor hemorrhagic. The softer parts, upon section, show no other explanation for their softness than a looser texture that may have been due to edematous infiltration.

#### MICROSCOPY

I began the histological study of my first case (1911) with the clinical diagnosis of sarcoma botryoides vaginae already made, expected the microscope to show sarcoma, and, though finding it atypical, persisted in regarding it as sarcoma. But during the interval of 20 years my ideas had changed and my approach to the present case was correspondingly different. I was now looking for evidences by which to prove that the lesion was a "mixed tumor."

I have carefully reviewed the old sections made from the tissue of the first tumor, and am certain that were I seeing them for the first time, and without my present preconvic-



Fig. This shows (1/4 natural size) front view of the tumor mass that projected through the vulvar opening. The perpendicular separation is on occasion through the entire tumor mass. The lateral lines are natural separations between lobules of the tumor.

tion that it was a mixed tumor. I should again reach the conclusion of 20 years ago and describe it as an edematous, and probably myxomatous, spindle cell sarcoma (Botryoid sarcoma).

Sections made from the various blocks of tissue taken from the present tumor are very disappointing in their simple histology. The fundamental structure was edematous (myxomatous) delicate fibrillar tissue much resembling that of a nasal polyp. Some areas contained relatively few and inactive cells, others greater number of cells, some of which are mitotic, while still others are composed entirely of cells with hyperchromatic and mitotic nuclei (Fig. 4). The cells, for the most part, were long delicate spindles, though here and there one encountered shorter spindles, and occasional areas of what seemed to be round cells. Near the surface there was much necrosis and keratin with characteristic inflammatory cellular infiltrations. Again the histology served to confirm the diagnosis of spindle cell sarcoma.

But the sections cut from block of tissue taken from the part mentioned as showing atypical cells supposed to represent one of the lobes presented some elements that should not be overlooked and may be significant.

Below the skin, which was all preserved, and free from neoplastic infiltration, though its corium was infiltrated with inflammatory cells, the tumor became edematous, and tumor cells, nearly all long slender spindles, began to appear. Among them were occasional giant cells that seemed to be of two kinds. Those nearest the surface are usually of rounded shape and resembled foreign body giant cells which they probably are, while some of those more deeply situated are elongated, the most

deeply situated among the tumor cells, very long, with the nuclei sometimes collected near the poles, sometimes distributed along a band of cytoplasm of uniform width and pronounced eosinophilic reaction. Some of these giant cells resembled the disturbed sarcomatous elements observed in injured and supposed regenerating voluntary muscle. It seemed as though they might be rhabdomyoblasts, whose transformation into striated muscle fibers had been checked through the occurrence of the edema, necrosis, and infection. Hundreds of them were examined in the hope of finding some that might show striations but without success.

Further study of other slides from other parts of the tumor showed occasional similar cells and cylindrical oriented bands of fibrils, eosinophilic in reaction, but without cross striations (Fig. 5). If the published illustrations of sections of other tumors, elements appear very similar to those just described except that some among them were striated. Making allowance for the embryonal and diseased condition of the tissue, it seems reasonable to assume that the cells under consideration may have been embryonal muscle cells, and that the tumor as a mixed tumor (rhabdomyoma) though it is impossible to prove it.

From the clinical and morbid anatomical points of view there is no doubt but that my first and second tumors are identical, and it is probable they both belong among the "mixed tumors" referred to by Sweet and many others. But without the presence of indubitable muscular or cartilaginous elements or some other positive evidence of heterologous structures could they be correctly called mixed tumors? We shall return to this question later. For the present let the term mixed tumor be set aside and the lesions designated as Schwalbe has suggested *dysontogenetic tumors*.

Thus freed from the limitations necessitated by nomenclature and abandoning the idea that the dysontogenetic tumors must be botryoid or sarcomatous or mixed tumors, I next set about collecting all of the tumors reported in the literature whose apparent origin, clinical peculiarities, anatomical distribution or histological structure made it probable that they might be of use in forming an intelligent understanding of their own nature and origin as well as that of the whole group. A lengthy bibliography was thus assembled. Of the total of 56 references collected 41 were not available but 475 contributions were actually examined and as many as seemed worth while were read.



Fig. 2 Complete section through the entire tumor mass (1/3 natural size) showing the bladder with its inferior posterior wall destroyed by the tumor mass that projected into and nearly fills it the middle part of the urethra whose meatus cannot be seen because it opens into a sulcus on the other side of the tumor; the vagina whose entire wall is invaded thickened, and internally necrotic so as to result in an irregular space with a shaggy appearance as though studded with slender worms (thrombosed vessels), the rectum slightly flattened by pressure, but patulous and undisturbed by tumor invasion, the large mass that projected through the vulvar opening

Of this literature it was soon discovered that a considerable portion, consisting of reports of tumor cases hurried into the literature shortly after operation and before either the histopathological examination revealed their nature or the subsequent clinical history showed whether they were malignant or not was of very little value. Moreover, it contains many cases in which the identification of the tumors was either entirely wrong or very doubtful (endotheliomata etc.), and deals with the transformation of benign into malignant tumors (fibroids to sarcomata) as though such a change were a demonstrated and accepted fact.

A bewildering terminology, containing 110 different names, gradually built up, also made it extremely difficult to trace the dysontogenetic tumors through the literature as one did not know under what headings to seek for them.

But the result of these studies has been as fruitful as it has been interesting. Among the dysontogenetic tumors of the urogenital region, with which this paper has to do, many



Fig. 3 View of the tumor mass and adjacent viscera as seen from the intra abdominal surface (1/2 natural size). It shows the uterus anteverted and antelexed and bound to the bladder with tumor nodules upon its fundus. The ovaries are small and dark colored the other pale enlarged and the seat of a peripheral metastasis.

of which are distinctly mixed tumors there is a great divergence of appearance and structure. Many are very soft edematous, myxoid polypoid and cystic—"botryoid"—while others are firm dense fibroid muscular cartilaginous or even osseous. The extremes in the series appear to be entirely different types of tumors and, indeed they are as can be inferred from the numerous terminology. A "myxoma" is certainly not the same tumor as a "chondroma." It is not the quality of the tumor, but its mode of origin that makes it dysontogenetic. Many suppose that the very soft botryoid tumors constitute a variety *sui generis* but the botryoid or "grape-like" appearance only results from the amount of moisture the tumor happens to contain. Tumors of similar histological structure are sometimes dense and dry.

It has been thought that the botryoid tumors are peculiar to infancy or at least to early childhood. But Kaschewarowa-Rednewa observed one at 15, and another at 17 years of age, Steintahl one at 22 years of age and beginning with Spiegelberg, whose patient was 45 years of age, many cases have been reported in the fifth and sixth decades of life. Robertson having seen one at 69 years of age.



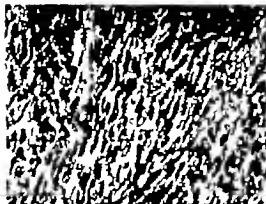


Fig. 4. Details of the structure of one of the densest and most cellular parts of the tumor showing the specific cell structure usually called sarcoma.

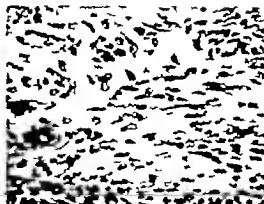


Fig. 5. Details of one of the softer parts of the tumor with two of the elongated eosinophilic structures thought to be myotic fibers, though some showed cross striations.

Dysontogenetic tumors have been observed to project as a small strawberry-like mass from the urethra or vagina at the time of birth to project into the bladder either from its walls, or from the prostate to grow in the vesico-vaginal septum extending into the bladder or into the vagina from anterior wall of the vagina, either high up or low down in either case eventually filling the cavity of the viscus with the tumor mass from the posterior wall of the vagina from the anterior lip of the cervix uteri from the endometrial tissue of the cervix or fundus of the uterus, or to occur as complications of uterine fibroids.

Some of the tumors make their appearances at fairly well defined ages. The botryoid tumors of the vagina are overwhelmingly more frequent in early childhood than at any other time while the similar tumors of the uterus occur chiefly in later life. Seventy four of the reported cases of botryoid vaginal tumors occurred in the first 32 years of life and none thereafter while of the similar uterine tumors only 33 were reported during the first 22 years of life and 39 thereafter. Forty two of the vaginal tumors were found in children of 3 years or less, against 5 uterine tumors of the same kind. Similar soft tumors of the bladder and prostate are almost peculiar to childhood.

#### ETIOLOGY

To understand what is here meant by dysontogenetic tumors, and why so many

different varieties and seemingly unrelated tumors are brought together and treated as though the same it is necessary to recall the embryology of the parts concerned.

At a very early stage of development when the yolk sac is being converted into the primitive intestine the allantois is given off as a diverticulum rapidly grows to a considerable size, and appears as a sac connected with the primitive gut by a tubular stalk that soon parallels the growing omphalomesenteric duct and ultimately becomes united with it to form the belly stalk of the growing embryo. Later the intra-embryonal part of the allantois becomes dilated into a fusiform sac, the office of which seems to be to receive the excrementitious products of the primitive urinary organs, the pronephros (?) and metanephros. At about the same time the pronephric ducts cease to be connected with the tubules of the pronephros, and become the ducts of the more important mesonephros, and as that organ progresses in its development grow caudally to open into the expanded part of the allantois, now the urogenital sinus. At a slightly later date on each side of the body along the genital ridge a fold of tissue curls inward to form a tube the upper end of which remains open with a flaring trumpet like expansion, while the lower part closes over to form a cylindrical tube the müllerian tube that elongates caudally descending toward the urogenital sinus where the approximated terminations

of both cause a slight projection in the posterior wall of the sinus, called the muellerian tubercle. These tubular terminations occupy a position internal to the wolffian ducts, or ducts of the mesonephros. All this takes place in embryos of about 10 millimeters. The later development and importance of these tubes differs in the different sexes. In males all of the tubes disappear except the extreme ends, the upper becoming the unimportant little cystic structure known as the appendix testis, and the lower the prostatic utricle, the vagina or uterus masculinus.

In the female on the other hand, the whole length remains to form structures of great importance. The upper trumpet shaped expansion becomes the imbriated extremity of the fallopian tube, the central parts become the oviducts, and the lower parts having received an investiture of mesenchyme, become fused at about the fourth month to form the vagina below and the uterus above.

If one recall the primitive and purely cellular character of the early embryonal tissues forming these structures, and picture the various consequences that might result from the ameboid wandering of some of the superficial cells, the dislocation of cells or groups of cells in the elongations, fusions, insertions, multiplications, and close approximations of the various groups of cells, of their growing importance at one time and waning importance at another, the admixtures and reinforcements that some of the cell groups receive from the myotomes, and the close relation to the subjacent sclerotomes and myotomes, it may appear to be more remarkable that the process of development takes place in so regular and orderly a manner than that it should occasionally meet with accidents resulting in dysontogenesis.

Dysontogenesis is the term used by Schwalbe to express accidents of development that may be followed by malformation or tumor occurrence. With the malformations we have, at present, nothing to do, our interest centers about the tumors, and the means of accounting for them.

The importance of dysontogenesis as a means of explaining the complex tumors was fully realized by Wilms, and brought out

clearly in his writing upon "Die Mischgeschwulste." It is certainly the most satisfactory theory by which to explain the origin of tumors characterized by the presence of heterogeneous tissues—"mixed tumors"—though some pathologists still prefer the old theory of metaplasia. Metaplasias probably do occur, but the theory has been much overworked.

Dysontogenetic tumors have no standards of histological structure. Some, like the two botryoid vaginal tumors of which mention was made previously, appear as simple tissue tumors and may be such, others are compounded of several tissues and are correspondingly complex. Perhaps all are really "mixed tumors" but failure to detect any tissue mixture makes it better to speak of them as ontogenetic or dysontogenetic.

It certainly seems paradoxical to speak of "mixed tumors" that are not mixed in so far as their histological structure is concerned. But how "mixed" must a tumor be to be classified as such? Among the tumors of the four organs here considered, the bladder, the prostate, the uterus, and the vagina, there seem to be all gradations between those composed of tissue of one kind only, and others with a highly complex combination of tissues. In all of these organs there are many reported cases of "mucous polyps," "edematous fibromata," "myxomata," "myxosarcomata," and "sarcomata," in which the structure seems to be so simple that no one seeing one for the first time, would ordinarily think of regarding it as otherwise. The first of the cases that came under my own observation seemed to be of a very simple structure and in consequence, was called "sarcoma." I did not realize until after I had studied my second case, how few, unobtrusive, and uncertain the rhabdomyoblasts, whose presence would change the diagnosis to mixed tumor, might be. In the cases reported in the literature one finds that the discovery of a very few striated muscle cells invariably leads to the diagnosis rhabdomyoma, a recognized type of mixed tumor.

The discovery of a single muscle cell is sufficient to make the tumor a rhabdomyoma. But if the muscle cells are very few and far between, they may not be found. It may therefore, not be possible to identify all mixed

tumors as such. Dymotogenetic is therefore a better term to employ.

Perhaps the matter can be better understood by reference to the other extreme of the series. The most complexly mixed tumors are found in the bladder and uterus and contain bone cartilage muscle nerve fibers and cells, adipose tissue occasional chromatophores, and of course numbers of blood and lymph vessels in variable proportions. Attempts to provide such tumors with appropriate descriptive names have resulted in the elaborate and meaningless terminology mentioned.

Where the diversity of the tissue is so great there is usually little question about the tumor being called a mixed tumor even though the author may prefer to account for the diverse tissues through metaplasia.

Cartilage is one of the most variable of the tissues found. In many of the uterine and vesical tumors it is absent in others the quantity is small in still others there is so much, and so little else that the tumors have been described as chondromata chondrosarcomata osteosarcomata etc.

It has been suggested that the age of the patient in whom the tumor occurs has something to do with the differing tissue components and their proportions. In general, the older the patient the greater the variety and the better the differentiation of the component tissues. The 74 reported cases of the very soft and simple botryoid tumors of the vagina all occurred before the twenty second year and the only heterologous elements found in them were striated and unstriated muscle cells some nerve bundles, and occasional unaccountable epithelial cells. Of 64 vaginal tumors a single one Mann's case 3 years old contained cartilage.

Of the 77 vesical tumors collected 6 occurred before the twenty second year and nearly all were very soft and simple much like the vaginal tumors. Of 48 prostatic tumors 38 occurred before the twenty second year and most of them were very soft in consistence and simple in structure.

But age alone does not adequately explain the structure for soft botryoid tumors of the uterus rarely occur until much later in life. Of 274 uterine tumors 34 of which occurred

before the twenty-second year of life only 22 were soft botryoid tumors while 39 similar tumors occurred after that age the oldest patient being 69 years of age.

The presence of heterologous tissue elements constitutes the characteristic feature of the mixed tumor and their presence is most satisfactorily explained by assumed early accidental dislocations of embryonal cells and their inclusion among others retaining their normal positions.

The cells thus dislocated may be conceived to meet with any one of the following fates: (1) the dislocated embryonal cell or cells may be suppressed and extinguished by the more vigorous growth and development of the normally situated cells (2) they may continue to live and complete their own differentiation in the abnormal environment at the same time as the normally situated cells, with the occasional occurrence of such congenital anomalies as the presence of striated muscle fibers in the myometrium etc (3) they may remain latent, alive and potentially vegetative for any length of time and at any moment initiate the growth of a tumor.

Some imagine that the dislocation supposedly taking place at a very early period of embryonal development, when both the normally placed and the dislocated cells are equally potent must inevitably show itself through immediate malformation or tumor development. It may but rarely does so. In the cases reported by Dehnborn and Garode, in each of which striated muscle fibers were found in the myometrium of an otherwise normal uterus, it may be assumed that both normally and abnormally placed cells developed simultaneously. In those cases reported by Martin Williams and Bowers in which the child was born with a vaginal tumor already in existence and projecting from the vulva, the two may have developed simultaneously the misplaced tissue excessively. Five of the reported vaginal tumors made their appearance within a few months and 10 others within a year after birth. But it is not necessary for them to appear so early for supposedly similar uterine tumors did not appear until after the fiftieth year of life. Presumably embryonal cells can and often do remain latent and

potential for many years, as is evident in the case of "uterine fibroids," about which more will be said later

Dysontogenetic tumors may not all be the result of embryonal dislocation. Some are homologous, and consist of, or are derived from, tissue elements normal to the part in which they occur. To explain them is one of the great problems of oncology, and, as yet, no explanation has been found generally satisfactory.

Cohnheim, who seems to have given the most rational theory, has been much misunderstood and much misquoted. He supposed that in the embryonal formation of each of the tissues, more cells are furnished than are actually needed, so that among those that develop and differentiate some are left over as though to serve for future emergencies—regeneration, etc., as they retain the potentialities of future development into normal tissue, so also, they possess the potentiality of tumor development.

If the edematous fibromata, mucous polyps, myxomata, etc. with which the tumor series begins, be as simple as they appear, they may have their beginnings in residual embryonal cells normal to the part, but not used up in its development. If dislocated heterologous embryonal cells accidentally included in any part explain the occurrence of a complex tumor, there is no reason why homologous embryonal cells belonging to it should not explain the occurrence of a simple tumor. The only remaining question would seem to be the possible presence of such superfluous cells anywhere. Perhaps this matter may be cleared by a brief consideration of the "uterine fibroids."

Uterine fibroids—leiomyomata or leiomyomata—are very common tumors, whose origin was for a long time assumed to result from the active vegetation of some of the cells of an originally normal myometrium. If the tumor was single, it was even imagined that it might result from an abnormally acquired vegetative activity of a single muscle cell, when, as was frequently the case, the tumors were multiple, of scattered cells. No explanation of the remarkable fact that only occasional muscle cells thus misbehaved was ever

given, nor was it remarked that all of the cells never became simultaneously vegetative with hypertrophy of the entire myometrium and a resulting gigantic uterus. Von Recklinghausen pointed out that the development of the tumors might be referred to defects in the fusion of the muellerian ducts to form the uterus, some of the myoblasts designed to form the myometrium then becoming accidentally displaced and remaining sequestered until, at some future time, they began to multiply, eventuating in nodes of muscular tissue enclosed in but not a part of, the uterine body, and so became tumors.

If true, this proves that embryonal muscle cells, at least, can be sequestered, and may remain latent in the surrounding adult tissues until, many years later, the growth of a tumor reveals their unsuspected presence. Such tumors are dysontogenetic and homologous.

But many fibroids, though apparently simple in histological structure, behave unexpectedly, and may manifest clinical malignancy, through rapid growth and metastasis. In such cases it is usually only one of several fibroids that shows this change, and not infrequently it is only some of the cells of the fibroid that assume the excessive vegetative growth, so that the behavior of those cells is, with respect to the tumor, exactly like that of the sequestered embryonal cells in the uterus was with respect to the myometrium. Curiously enough this abnormality of the tumor has received exactly the same explanation that was originally accorded to the occurrence of the fibroids themselves. It is supposed to depend upon an acquired change in vegetative activity on the part of one or a few of the tumor cells. But may it not rather depend upon the presence of still other remaining embryonal cells?

It was early discovered that fibroid tumors were occasionally complicated by the presence of endometrial tissue with its characteristic epithelial tubules, and such tumors were called "adenomyomata."

The endometrial elements were difficult to account for, and elaborate theories were propounded, as, for example, that as it grew, the fibroid dislocated, and dragged some of the subjacent endometrium into its own sub-

stance where it grew *pari passu* with the tumor. How much easier it seems to account for the presence of the endometrial tissue on the ground of dyontogenesis, and remembering that the muellerian ducts not only furnish the material for the formation of the myometrium, but also for the endometrium, assume that in the defective amalgamation of the tubes, both embryonal myometrial and embryonal endometrial tissue elements were dislocated and sequestered the subsequent complexity of the tumor resulting from the later and simultaneous development of both. But this is again a homologous tumor and though it may very well be dyontogenetic cannot in its usual meaning be called a mixed tumor.

It is interesting because unusual to observe the presence of heterotopic tissues both in the uterus, and in tumors of the uterus. In my collection of microscopic slides there is a section of what at first appeared to be a perfectly formed and normal uterus, upon one side of the body of which there was a pale spot about 1 centimeter in diameter. Upon examination it proved to be a mass of adipose tissue. There is no reason to regard it as a tumor: there was no enlargement. It seems simply to be a malformation that resulted from the dislocation and inclusion of some neighboring lipoblasts among the myoblasts out of which the uterus was developed. It did, however, cause a defect in the continuity of the myometrium, and in case of pregnancy might have predisposed to rupture of the organ.

The presence of adipose tissue in the uterus has frequently been observed and takes numerous forms. Lebert has reported a case of adipose tissue in the wall of the uterus. Wilkenson and Brockman and T. Smith have all referred to Specimen No. 3001 in the museum of St. Bartholomew's Hospital in which there is an encapsulated lipoma in the wall of the uterus near the fundus. Sitzenfrey reported a case in which adipose tissue ramified among the muscular bundles of a leiomyoma of the uterus. Glass found adipose tissue in 11 out of 938 leiomyomas. Strofinski observed a small lipoma of the anterior lip of the cervix that hung down as a covering of the os, so as to cause sterility until removed.

In a paper published in 1906 A. G. Ellis placed the number of reported cases of true lipomata of the uterus at 11.

The appearance of heterotopic adipose tissue in the uterus, sometimes in the form of an indefinitely circumscribed mass in the myometrial substance, sometimes in the form of a circumscribed and encapsulated tumor and sometimes ramifying in all directions among the muscular bundles of a fibroid, certainly seems to be the result of a developmental disturbance rather than of a metaplasia.

The same is true of other heterotopic tissues. R. Meyer found a mass of cartilage in the cervix of an otherwise normal fetal uterus. Gaileroni reported the discovery of a cartilaginous nodule in the body of the uterus. In 3 of Hartfall's cases of mixed tumors cartilaginous nodules were found in endometrial scrapings.

The occurrence of heterotopic bone is rare. It is occasionally found in vaginal tumors, in uterine fibroids, and in the complicated mixed tumors of the uterus occurring in later life. In 2 cases, those of Benecke and Shattock, it has been reported as occurring in bladder tumors. Benecke's patient was a man 71 years of age, in whose bladder there was a mass the size of a small apple, the center of which was bone with well defined Haversian systems, surrounded by a mass of fibrochondroid tissue. Other tumors containing bone have been reported by Meyer, Pernici, Planensattel and Wolf.

Nervous tissue is the rarest of the heterotopic tissues to be found in the region under consideration. Amann in an infantile vaginal tumor found striated muscle, solid strands and gland-like alveoli of epithelial cells, bundles of thick nerves and ganglionic nerve cells. The most remarkable tumor of this kind was reported by Kleine whose adult patient had a medium sized degenerated fibroid of the fundus of the uterus and entirely separate from it, in the lower part of the uterus, projecting externally and forming a rounded mass almost the size of an egg, an independent tumor mass, of paler color made up entirely of well formed and fully medullated nerve fibers. From the standpoint of the present

discussion this appears to be of immense importance, for not only is the tissue heterologous, but also adult, and of a very peculiar kind, impossible to account for through metaplasia. How could a tumor mass of nerve fibers thus occur? The most simple explanation seems to be the assumption that at a very early stage of embryonal development, there had been dislocation of neuroblasts, that had multiplied excessively, differentiated, giving off fibrils as they matured so far as medullation was concerned. The nerve fibers thus formed, having nowhere to go, and nothing to do, had persisted while the cells by which they were formed had degenerated and disappeared. In large retroperitoneal ganglioneuromata it is not uncommon to see the sympathicoblasts multiplying freely, partly differentiating into ganglion cells, and these undergoing vacuolar degeneration and disappearing, leaving their fibrils and surrounding Schwann cells to form the bulk of the stroma of the tumor.

A number of the tumors found in the region under consideration have been described as melanotic (melanotic sarcomata). The cases reported by Boldt, Graefe, Matthews, Smith and Luch, and Stefani, all occurred in adults. It was at first conceived to be impossible that these tumors had anything whatever to do with the principles of dysontogenesis or embryonal dislocation. There seemed to be no reason for assuming that melanoblasts either belonged in the parts or were in the neighborhood. But since it has been shown that melanoblasts may be but satellite cells of the nervous system, and as nervous tissues are occasional components of dysontogenetic tumors, it becomes quite possible.

It may occur to the reader that if the theory of dysontogenesis with the dislocation of embryonal cells be granted, definite distribution of the dislocations must result from the anatomical relations of the embryonal parts. That is correct and it was pointed out at the beginning of this paper, that there is a fairly regular distribution. The tumors are most frequent in the uterus, then in the vagina, then in the bladder, and lastly in the prostate. They occur very rarely in closely adjacent regions. Guersant's botryoid tumor is said to

have occurred in the vulva, Lannois's tumor in the prepuce of the clitoris, Serafini's tumor seemed to arise from the urethra, and Rokitsansky's tumor, occurring in a lad of 18 years, was near the anus. More of the uterine tumors were of the corpus than of the cervix, more of the vaginal tumors arose from the anterior wall than from the posterior wall, while a very few were scattered over the vaginal wall as though multicentric. Vesical tumors were much more frequent in the region of the trigone than elsewhere. The few and slight departures from these positions may be attributed to the growth movements of the embryonal structures, and to the ameboid movements of the dislocated cells, that may be imagined to be striving vainly to regain their normal relationships.

The histological variation of the tumors, and the differing proportions of their tissues result from the kind of cells dislocated, the number of cells dislocated and the ease or difficulty with which their evolution is effected in the abnormal environment in which they find themselves.

No one has the slightest information as to the forces that initiate or determine tumor growth. In some cases it seems to be related to hormonal activities, as in the case of uterine fibroids, in others to general or local metabolic variations. It is hard to refer ontogenetic tumors to "irritation." But, however it begins, once the neoplastic growth is under way, variations in the results may be expected in consequence of the number, kind, and position of the cells forming the primordium of the tumor, and their possible interference with one another.

Should the tumors arise from homologous residual embryonal cells of one kind, there will be only one type of tissue, and the tumor will be simple, if from several kinds of cells the tissue resulting from the most successful cells will preponderate. Where there are several types of cells and resulting tissues that possessed of greatest vegetative activity will preponderate unless it meets with some kind of mechanical or chemical interference. It can, at least, be imagined that that tissue which gets and keeps the best start will preponderate over all others, and its predominance may not

only be quantitative but qualitative. The dominant elements, through multiplication or differentiation or both may so interfere with others as to suppress their evolution and maintain them in the embryonal cellular state.

For this reason an overwhelming number of the tumors contain larger or smaller numbers of undeveloped and unidentifiable cellular elements that lead to the tumors being classified among the sarcomata. The term "sarcoma" appears so constantly in the nomenclature of these tumors as to give the impression that there is full justification for it. Indeed, the clinical behavior of the tumors seems to support this view for almost without exception they are malignant, recur again and again and eventually destroy life.

#### REFLECTIONS UPON THE NATURE OF SARCOMA

At first glance it may seem as though the discussion of this question is widely removed from the scope of this paper but it is unavoidable for without it much of importance will have to remain in the dark.

Etymologically the Greek word *sarcoma* means simply fleshy swelling or lump of flesh. The word is in such every day use among clinicians, pathologists, and histopathologists as to suggest that it is well understood. As a matter of fact it is so vague as to have very little real significance. By various authors different definitions are given but nearly all agree upon the following general principles: (1) sarcoma is a malignant tumor; (2) it occurs chiefly in the young; (3) it consists essentially of cells; (4) the cells are of mesoblastic origin; (5) the cells are of embryonal type; (6) they represent the early form of the connective tissues.

Three different conceptions enter into the wording of most definitions: malignancy which is clinical; cellular structure, which is histological; and mesoblastic derivation which is embryological. Not one of these is constant.

*1. Malignancy.* It is extremely variable, and runs the whole gamut from tumors that are quickly and widely metastatic and fatal, through those that grow slowly and recur again and again after removal, to those that seem to be cured by a single excision. Tumors as variable as this cannot all be the same.

*a. Cellular structure.* The cellular variations are remarkable. There are small round cell tumors, oat-shaped cell tumors, small spindle cell tumors, large spindle cell tumors, mixed cell tumors, in which there are both round and spindle cells, large round cell tumors, irregular cell tumors, and pigmented cell tumors. All of these were said to be sarcomata, until it was discovered that a good many of them belonged in other categories. But why were they at first and for so many years regarded as sarcomata? Simply because they were cellular tumors, the cells of which could not be identified. The first subtraction from the group probably began with Marchand who found little globes of cells, having a central tuft of delicate fibrils, in a small round cell sarcoma of the adrenal region, and pointed out that the cells thus arranged and characterized were undoubtedly "neuroblasts, and slightly more advanced in evolution than the generality of the cells that were neurocytes." Many other tumors of the same kind have since been found but they are no longer spoken of as sarcomata through ability to identify their cells; they have now become neurocytomata and neuroblastomata, and with the more correct understanding of the cells it became necessary to modify the embryological conception of the tumor. The blastodermic derivation of nervous cells is ectodermal, not mesodermal; the cells are not embryonal connective tissue; they are nerve cells. That the tumors are clinically highly malignant makes no difference; they have ceased to be sarcomata, and have become malignant neuromata.

Large tumors of the anterior mediastinum composed of small round cells were some years ago called small round cell sarcomata; then with improved cytological technique were more specifically called lymphosarcomata. But recently ideas changed with respect to the embryonal derivation of the thymus, and its small cells began to be regarded by an increasing number of embryologists and histologists as epithelial and ectodermal in origin when of course it at once became necessary to change the name of the tumors, which are now generally known as thymomata, and regarded as belonging in the carcinoma class.

Certain "small cell" tumors of the lung and of the prostate were for years unhesitatingly regarded as sarcomata, but with more careful study have been recently reclassified as small cell carcinomata. It seems, therefore, that it is chiefly when the real type and derivation of its cells are not known that a tumor is a sarcoma. So soon as they can be correctly identified, the tumor is removed from the rapidly shrinking sarcoma class. This is not only true of tumors composed of small round cells, it also applies to those composed of spindle cells. Tumors occurring along the course of nerves, and composed of long spindle cells were formerly called sarcomata. The cells were thought to be connective tissue cells, and of mesodermal origin, but with modern methods of study, are now believed to be derived from the cells of Schwann, and of ectodermal derivation. Such tumors are now called Schwannomata, and, of course, are removed from the sarcoma group. Other examples might be given did space permit.

3 *The mesoblastic derivation of the cells.* It is easy to declare upon academic grounds alone that each tissue can be referred to one or other blastodermic layer, and therefore, any tumor having a structure seemingly identical with it, must be derived from the same blastodermic layer, but in practice it becomes almost impossible.

Evidences of this difficulty have already been cited in the case of the neurocytoma, the thymoma, the Schwannoma, and the carcinomata of the lung and prostate. But it obtains in many other cases. Many tumors, today unhesitatingly described as carcinomata, were, in the past described as "alveolar" sarcomata, and supposed to be of mesoblastic derivation, upon the purely theoretical ground that there could be no ectodermal derivations in those parts of the body in which the tumors occurred. We now recognize the occasional heterotopic presence of abnormal tissue elements of unexpected blastodermic derivation almost anywhere.

Tumors of the urogenital apparatus perplex us because all of the epithelial elements are supposedly mesoblastic. Shall carcinomata of the uterus be called sarcomata because of the blastodermic derivation? Many tumors of the

ovaries and testes, being almost purely cellular are impossible to classify because the cells lack sufficient characters by which to classify them.

From the time of Virchow until quite recently, all of the tumors of the melanoma group were known as "melanotic sarcoma" because the tumors were purely cellular, malignant, and composed of cells, which though pigmented were so indefinite as to be regarded as mesodermal in origin and of connective tissue type. Only recently, and largely through the work of Masson, it has come to be generally considered that melanoblasts are cells of ectodermal derivation, belonging in the category of satellite cells of the nervous system, and that the pigmented tumors are therefore not sarcomata at all.

But there are many to whom Cohnheim's theory of residual embryonal cellular material does not appeal and who look for some other means by which to account for the embryonal or embryonal appearing cells in the tissues of tumors. A theory popular at present is that of Hansemann and is described as *anaplasia*. It teaches that through rapid multiplication of cells their specialization and essential characterization are gradually lost, so that with each generation of multiplying cells there is a more and more complete return to the embryonal appearance and behavior. Whether or not such a change is possible is uncertain. It could apply only in cases in which the cell differentiation did not preclude multiplication as it often does. Under every kind of adverse condition highly specialized cells die and disappear. Evidence in support of the theory of anaplasia is supposed to be manifested by certain uterine fibroids that grow rapidly and finally show themselves to be clinically malignant (metastatic).

Fibroids when examined present interesting variations in structure. Some are purely muscular—there is naturally always some interspersed fibrillar tissue surrounding and supporting the blood vessels just as is the myometrium—and appear to be finished and inactive neoplastic formations, while in others one or several foci may be found in which the cells are vegetating, and show such modifications as are incidental to multiplication—larger



size metachromatic nuclei, karyomitotic nuclei etc. In a few cases the whole tumor may seem to be thus engaged in rapid growth and from some such tumors occasional cells may be distributed by way of the blood stream, with resulting distant metastases. Such malignant metastatic tumors are usually called leiomyosarcomata, though there is no valid reason for the use of the term sarcomata, the cells are muscle cells and the tumors are in reality malignant myomata.

In another group among the muscle cell bundles, either widely distributed, or locally collected, strands or groups of small spindle cells may be found. These are totally unlike muscle cells, and in no manner traceable to them. Their rapid multiplication results in an entirely new type of neoplastic tissue exactly like spindle cell sarcoma as seen elsewhere and in metastases bearing no resemblance whatever to muscular tissue. These tumors are always called spindle cell sarcomata, and with greater justification. Here therefore are two entirely different conditions, called by the same name one of undoubted myogenic origin the other apparently not. Unfortunately this has given rise to the supposition that the muscle tissue, through anaplasia has changed into connective tissue and so undergone a sarcomatous change. In the first instance there was no change the tumor originally consisted of muscle and although its cells rapidly multiplied, they remained muscular cells. In the second instance however the tissue through the dissemination of which the metastasis took place was of an entirely different kind, that only by stretch of the imagination can be regarded as having originated by anaplasia from the muscle cells. It would be strange if rapid multiplication of the cells should result in anaplasia in one case and not in another!

It is not unusual to find among multiple fibroid tumors some that present the usual muscular structure and some made up partly of muscle and partly of small spindle cells like those described as characteristic of spindle cell sarcoma. If we are willing to admit the probability of the adenomyomata being dysontogenetic, and the result of embryonal endometrial inclusion it is difficult to escape

the conviction that the other varieties may originate in the same manner. There are also occasional malignant and metastatic fibroids in which the two types of cells grow together both appearing in the metastases. These are often adduced to prove that the one type of tissue has transformed or is transforming itself into the other and transition steps are some times pointed out but nothing is more hazy and arduous than an attempt to derive one tissue from another by pointing out the intermediate steps. It is more probable that the transformation is imaginary and that the different tissues have existed side by side as the result of dysontogenesis.

But what is the true nature of the cellular tissue the presence of which characterizes sarcoma? It seems probable that it is residual, embryonal cellular tissue sequestered or dislocated. What kind of tissue antecedent it is may never be discovered because it has not evolved. It is simply *undifferentiated cellular substance*.

It is because of the presence of more or less of such undifferentiated cellular substance that the great majority of the mixed tumors have been called either sarcoma or some variety of sarcoma.

This brings up the last question, what is sarcoma? Is it not possible that it is nothing but vegetating proliferating undifferentiated residual embryonal cellular substance sequestered either in its normal environment or dislocated from it until traumatism, metabolic or hormonal stimulation, or some other cause determines that it shall result in a tumor?

Looking over the literature one finds that inability to identify the character of the cells in a tumor has sometimes resulted in the grossest errors of diagnosis and frequent abuse of the term sarcoma.

In 1894 a tumor with a remarkable variety of cells large and small single and syncytial such as I had never seen, came under my own observation. In the absence of any familiar appearances and by exclusion it was described and reported as a large round cell sarcoma of the uterus. Years afterward, "syncytioma malignum" began to receive attention as a new variety of tumor and

remembering the peculiarities of that just mentioned, I reviewed the slides, and found out what it was. The confusion becomes even worse if the cells seem to the pathologists to resemble those of some unusual though recognized type. In this way many tumors have been described as "endotheliomata" that upon renewed study resolve themselves into entirely different types of tumor. A review of the illustrations in some of these publications may be sufficient to show that commonplace carcinomata have sometimes been described under this doubtful and ambiguous term "endothelioma."

Not long ago two tumors were brought to me as "sarcomata" of the vagina. They were of entirely different histological appearance though each was essentially made up of spindle cells. One had occurred upon the anterior vaginal wall and had promptly recurred after operation, while the other, located upon the posterior vaginal wall showed no return. Careful histological study of these two tumors showed each to be made up of easily identified elements. The former consisted of small spindle cells, so arranged that the whole structure seemed to be made up of little rosettes, in the centers of which were occasional tangles of very delicate threads, almost unmistakable evidence of the nervous origin of the tumor, which was in all probability a malignant neuroma. The other tumor was composed of larger, longer, and more slender parallel spindles that usually assumed a wavy course with frequent palisades of nuclei, and other appearances familiar to all who have had experience with the Schwannomata. The final identification of these tumors came as a surprise to the first observers, but had they known or remembered that tumors of the vagina, bladder, and uterus containing ganglionic nerve cells, medullated and unmedullated nerve fibers, had been recorded, the surprise would have been less.

#### DIAGNOSIS

The histopathological diagnosis of the dysontogenetic tumors is easy or otherwise according to their structure. When the tumor consists of a variety of tissues, some distinctly heterologous (mixed tumors), there may be

no trouble, but when its structure is simple, it becomes more and more difficult to be sure of its nature and in some cases may be purely a matter of opinion. This is particularly the case with the vaginal, vesical, and prostatic tumors of infancy and early life, described in the literature as edematous fibromata myxomata or sarcomata, and with the uterine fibroids. In spite of what has been said some pathologists will no doubt prefer to regard the simple appearing tumors as simple "blastomata" and "sarcomata," but it is hoped that the significance of their relative positions as extremes in a long series of tumors of increasing complexity will not be disregarded.

#### PROGNOSIS

All dysontogenetic tumors must be regarded as potentially malignant. The malignancy shows itself in different ways in different tumors and at different ages. The botryoid tumors of early childhood show it through repeated recurrence, and local invasion followed by obstructions, ulcerations, necroses, infections, and hemorrhages. Metastases are rare. Dugge saw a pleural, and Sutton a pulmonary metastasis from vaginal tumors of little children, the case herein reported had local metastases upon the peritoneal surface of the broad ligaments ovaries, and the fundus of the uterus.

The tumors of adults are somewhat more apt to be metastatic. Delagenière and Beauchef saw a tibiopectoral metastasis from a uterine tumor containing bone and cartilage in a woman 54 years of age, Hartfall saw two adult intra-uterine tumors containing cartilage cause death through metastasis to the lungs, Heddaus saw a metastasis to the pleura from a botryoid tumor of the uterus in a woman aged 48 years, Graefe saw a patient 22 years old with melanotic sarcoma of the vagina die with metastasis to the lungs, one of Kaschewarowa-Rednewa's cases of botryoid tumor had a metastatic nodule in one kidney, Smith saw metastatic nodules in the great omentum, Stefan reported a case of melanotic sarcoma of the vagina in a woman 68 years old, who died with metastasis to the liver, Graefe also saw a woman aged 22 years, with a melanoma of the vagina die of pulmonary

metastasis and Rein saw metastatic nodules in the pelvic lymph nodes and wall of the vagina in a woman 21 years of age with sarcoma enchondromatodes arborescens colli uteri. But, all told, excepting those cases described as sarcomatous degeneration of uterine fibroids there seem to be only about a dozen cases of metastasis near and remote recorded in the literature.

#### TREATMENT

When the usual course of the tumor is, as in the case of the botryoid type repeated recurrence, local invasion of the surrounding tissues, and death from obstruction of the urinary passages, little can be expected from operative treatment, and in almost all cases it fails, and the patient dies. In very rare cases, and when as sometimes happens, a vaginal tumor is situated upon the posterior wall operative removal may succeed. The recovery that followed a second operative removal in one of Frick's cases (Schuchardt's case) is attributed to that tumor having been so situated. This patient was living and well 10 years later. Edsbohlis has reported a case of adult vaginal sarcoma that remained well for 3 years and 3 months after operation but in almost all of the reported cases the patients have died.

Treatment by X-rays and radium seemed to offer a better means of attack, but experiences with them have not been followed by the happy outcome that was hoped for. The patient reported by Halle, Grael and Veau who was 2 years of age when the treatment for a botryoid vaginal tumor was begun, is said to have been kept alive for 7 years through repeated radium treatments, though she finally died of the tumor. Adler, Doederlein, and Reisch have each reported a case "cured" through courses of radium treatments, but through private correspondence I learned from Adler that his patient finally died of sepsis—one of the natural terminations of the tumor. Doederlein kindly wrote me that his little patient was alive and free from recurrence a year after the treatment was begun, but the period is, of course, entirely too short to make sure what the final outcome may be. Reisch probably failed to receive

my letter as he did not answer it. The present condition of his patient is, therefore, not known though again the time that elapsed between the treatment and its reported success is not sufficient to convince one of the future safety of the patient.

A considerable number of recoveries after operation for the removal of malignant leiomyomata are on record, but inasmuch as there are no satisfactory microscopical criteria for determining the malignancy or benignancy of such tumors and as many of the reported cases had never been microscopically examined, it is impossible to tell what the tumors really were.

#### CONCLUSIONS

A considerable and miscellaneous variety of tumors that develop from, or in close proximity to those embryonal structures that enter into the formation of the urogenital sinus, are most easy to account for upon the basis of origin through dysontogenesis.

The most characteristic of these tumors, being composed of several different and easily identified tissues, some of which are foreign to the part—heterologous—are readily assigned to the class known as mixed tumors.

Others of simple structure and therefore not appearing to be mixed tumors, through their localizations, clinical appearances, and behavior seem also to belong in the dysontogenetic group.

The frequent occurrence of the tumors at a very early age, and the distinctly embryonal nature of their tissues suggest origin from residual embryonal cellular material such as Cohnheim first pointed out. Almost all of the tumors contain larger or smaller numbers of undifferentiated embryonal cells, of which the true nature is obscure.

When a large number of the tumors is arranged in series the structure is found to pass by gradations to greater and greater histological complexity and the appearance of heterologous tissues. It seems reasonable, therefore to assume that the complexity and heterologousness depend upon the dislocation and inclusion of cells or groups of cells of the primitive embryonal substance, and their subsequent development in the heterotopic posi-

tion Thus dysontogenesis may account for all of the various tumors discussed

The tumors are all potentially malignant, and most of them actively so

It is believed to be an error to think of these tumors as varieties of sarcoma and their relation to sarcoma and the probable nature of sarcoma are discussed

The literature of the subject is so confused through complicated terminology incorrect identification of individual tumors premature publication of cases declared to be cured after operation or other treatment, the designation of certain tumors—uterine fibroids—as malignant, from histopathological appearances the exact significance of which is not under-

stood and may be in no manner indicative of malignancy, that a careful analysis of it has resulted in little of value

Except in the case of the tumors in the group of "uterine fibroids," very little seems possible in the way of successful treatment Surgical operations irradiation by X-rays and radium alike usually fail to prevent recurrence or to save life

Note—The original manuscript of this paper was accompanied by numerous tabulations, lists, and classifications and followed by a bibliography comprising 513 titles and references As they may be valuable for reference to some of the readers of the paper, and as it required several years to collect and arrange them, copies will be placed with the American College of Surgeons and the College of Physicians of Philadelphia where they may be consulted

# CLINICAL SURGERY

FROM THE GLASGOW MEMORIAL HOSPITAL

## TRANSPLEURAL NEPHROPEXY

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IN 1913 Mr Maynard published his classical work *Practice and Problems in Abdominal Surgery*. In that book he briefly but masterfully described in Chapter XXII his operation for the fixation of the abnormally mobile kidney. He had employed that method for some years prior to publication, that account of the operation may therefore be taken as the result of his mature experience.

Having had the privilege of being his assistant for some years, I have had the advantage of acquiring direct from the author the details of the operation as performed by him. Possessing now at this date a comparatively large personal experience, and having introduced several modifications of the original technique, the time appears opportune for the presentation of a further communication on that subject. Following upon a few preliminary anatomical, physiological, and etiological remarks, I will endeavor to describe the operation as it is performed at this date.

### ANATOMY

The structures directly involved in the performance of this operation are the pleura, the diaphragm, the structures occupying the intercostal space, the kidney, and the posterolateral abdominal wall. The lung will be described because it might be involved but it should not be I will endeavor to describe the parts with relative accuracy in the order in which they are encountered during the performance of the actual operation.

*Posterolateral abdominal wall.* The incision is made transversely half an inch below the level of the tip of the twelfth rib, skin, subcutaneous tissue, superficial and deep fascia, posterior layer of the lumbar aponeurosis, external oblique, internal oblique and transversalis muscles are divided in order named, when the pararenal and perineal fat are reached and cleared aside.

*The tria of Petit.* Base is formed by the middle third of the iliac crest, its apex by the overlapping of the external oblique and latissimus dorsi, its anterior boundary by the posterior border of the external oblique, and its posterior boundary by the anterior border of the latissimus dorsi. The roof is formed by skin and fascia and its floor by the internal oblique.

*Kidney.* The organ by means of which many of the waste products of the body are eliminated. The kidneys are situated postperitoneally, embedded in fatty areolar tissues mainly in the hypochondriac and epigastric regions, but they also extend to a variable extent into the lumbar and umbilical regions. It may be said that a considerable diversity of opinion exists as to their exact position and its normal variations.

In the adult the kidneys weigh  $5\frac{1}{2}$  ounces, and they are said in the adult to account for one thousandth and fortieth of the total weight of the body. In the infant they form one one hundred and twentieth of the total body weight. Their weight is said to be slightly less in the female. They are bean shaped and of a dark reddish brown color, slightly mottled by their grayish white, glistening capsule. Their component parts are two borders, two surfaces, and two extremities.

The posterior surface rests upon the peritoneal fatty areolar tissue, which rests upon the fascia covering the diaphragm, quadratus lumborum, and psoas muscles, the eleventh and twelfth ribs, and the transverse process of the first and second lumbar vertebrae and sometimes that of the third, the twelfth dorsal, the eleventh and thirteenth thoracic nerves along with the anterior divisions of the first and second lumbar arteries and veins.

The external renal border is convex in its upper third and the right kidney is in contact with the liver, its lower third with the colon, and rests upon the aponeurosis of the transversalis abdominis. The left is in contact with the pleura.

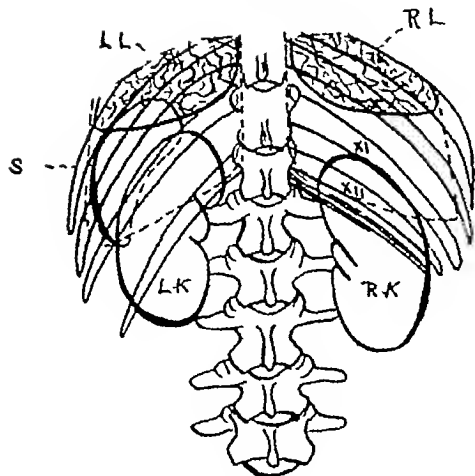


Fig 1 Diagram showing the posterior relations of the kidney

The internal renal border is concave, and in the case of the right kidney, is in close proximity to the inferior vena cava, that of the left kidney is 1 inch from the abdominal aorta. This border presents the hilum which is situated approximately in its middle third and has an anterior and posterior lip within which is the sinus occupied by the renal vessels and veins in the following order from before backwards: veins, arteries, ureter, nerves, and lymphatics. From above downward: right kidney, vein, artery, ureter, left kidney, artery, vein, ureter.

The arterial supply (Fig 2) is derived from the aorta, via the renal, suprarenal, spermatic or ovarian and lumbar. The right renal vein empties directly into the inferior vena cava, while the left, which crosses over the abdominal aorta, as a rule receives the ovarian or spermatic, according to sex, and in certain cases the inferior phrenic and suprarenal.

The nerve supply is mixed. Fibers of spinal origin are derived via the small and least splanchnic and vagus through the celiac plexus. The sympathetic supply is derived from the aortic nerve ganglion and celiac plexus.

The lymphatics are disposed in two sets, superficial and deep, and drain into the lumbar glands.

The kidneys may vary in form, size, position, and number. Any variety from the normal may be encountered. They may retain the lobulated form of infancy or they may be round and triangular as in the form of a horseshoe, thus forming only one kidney. One kidney may be very much reduced in volume, if so, as a rule the opposite is much larger. Variations in number are

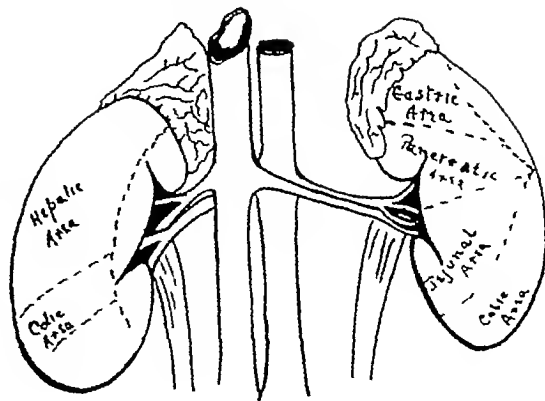


Fig 2 The anteroposterior relationship of kidney

comparatively infrequent, the horseshoe variety, being perhaps the most common, but one kidney may be entirely absent, or there may even be three! If a third is present then it is usually situated in a mesial position.

The kidneys are situated in the renal fossæ and maintained in that position by their relations with adjacent structures, the form of the fossæ, the fatty capsule, the perirenal fascia, and I hold much more than is generally believed, by the maintenance of normal intra-abdominal pressure. In passing, I believe variations of this are frequent in the female, but normally completely unknown in the male. The vessels and nerves forming the hilum also play a part, as does also its peritoneal associations.

The fixations are (1) the fatty capsule, (2) the vessels and nerves, (3) partial covering of peritoneum.

**Lungs** The right lung is larger and heavier than the left and is situated higher in the thorax for two reasons: because of the presence of the large lobe of the liver and in the absence of the heart. Thus the limits of the organ are: in the nipple line it reaches the sixth rib, and in the posterior scapular line the tenth rib. In the case of the left lung its lowest limit is the upper border of the eleventh rib. It is most important to remember those simple anatomical points.

Thus one can risk perforating the tenth intercostal space on the right side without, in the majority of cases, involving the lung, but one cannot go higher with safety than the eleventh on the left side.

**Pleura** The lower border corresponds in the nipple line with the eighth rib. In the midaxillary line the tenth rib on the left side and the ninth rib on the right. In the posterior scapular line with the twelfth rib, and in some cases with the

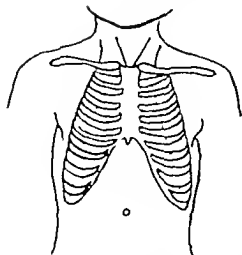


FIG. 3 The relationship of complementary pleural space

transverse process of the lumbar vertebra. The supplemental or complementary pleural spaces are best shown in the following diagrams (Fig. 3)

**Intercostal space.** Between the costal cartilages and the angles of the ribs you have the skin, overlying muscles and fascia, external intercostal muscle, intermuscular areolar tissue, with arteries, veins, lymphatics and nerves, internal intercostal muscle, endothoracic fascia.

It is to be particularly noted that posterior to the angles of the ribs, the intercostal vessels and nerves cross the intercostal space obliquely. This is probably the most important point to be noted because it is a good injuring the structures the needle carrying the superior suture must perforate the intercostal space anterior to the angle of the rib otherwise there is danger that these structures may be injured. If the proper needle be used however that danger is very remote, but in any case this space should not be utilized.

#### PHYSIOLOGY

It has been observed that the kidneys under normal circumstances have a definite anatomical position. Their disposition in that region is such that their attachments and relationships with their surroundings allow of a certain amount of definite and unrestricted movement. The manner in which they are anchored and the presence of a peculiarly disposed and relatively mobile fatty capsule protects them from any undue external influence of moderate severity. The presence of this shock-dampening elastic casing as the fatty capsule might be called allows unrestricted intra-

renal movements which unquestionably occur during digestion and other modifications of the system generally. Being situated in close contact with the main muscle of respiration the diaphragm, they are never at complete rest. Recognizing the fact that they are peculiar inasmuch as they may be regarded as being both secretory and excretory, very considerable variations in their volume are constantly occurring.

Intrarenal movements are these which occur during variations in blood pressure, digestion, stimulation of the sympathetic, and in the female during menstruation and pregnancy.

Intrarenal movements have been demonstrated by Roy and Cohnheim, using an oncometer. By means of this method it has been shown conclusively that the volume of the kidney varies rhythmically and continuously. Such being the case and recognizing the fact that the capsule of the kidney is in molecular continuity with the renal parenchyma, these intrarenal movements exert a certain amount of movement, slight though it may be of the organ in relation to its surroundings.

Extra-renal movements are those which occur in virtue of its anatomical position and may be classified as (1) respiratory (2) visceral (3) vertebral, and (4) muscular.

As it is in relationship both directly and indirectly to the main muscle of respiration, the diaphragm, a certain amount of mobility is created with each respiratory act. The intercostal muscles probably exert a slight secondary influence.

The right kidney is probably the more mobile of the two because of its close relationship to the liver. Mobility in the case of the left is not so marked because while it is more highly placed and has an extensive and intimate gastric relationship, its diaphragmatic association is weaker and there is a tendency to increased stability due to the anchoring effect of the tail of the pancreas inferiorly, the comparatively immobile spleen, and the shortness of the left renal artery. The peristaltic action of the large and small intestines has a definite effect.

In all the movements of the vertebral column there is a definite degree of renal movement probably more pronounced in full flexion.

Muscular action is most marked in people who use their lower limbs. In the trunk more or less fixed, such as bandmen, who, by the use of the lower limbs with the trunk rigid, bring into active use the iliopsoas muscle. Indirectly through violent action of the latissimus dorsi by fascial attachments, renal movements are produced.





In the acquired class the condition may be due to

- 1 Chronic cough
- 2 Constipation,
- 3 Cecal distention
- 4 Debility
- 5 Spinal curvature,
- 6 Renal enlargement due to—
  - (a) Calculus,
  - (b) Hydronephrosis,
  - (c) Pyonephrosis,
  - (d) Cyst,
- 7 Enlargement of adjacent organs—
  - (a) Liver
  - (b) Suprarenal capsule,
  - (c) Spleen
  - (d) Gall bladder
  - (e) Stomach,
  - (f) Colon,

8 Pelvic disease through the medium of adhesions to adjacent structures,

#### 9 Trauma

Trauma may be one or all of three varieties, or all three combined, but before any of them can be effectual there must be a congenital predisposition which may be partially or completely developed. If this predisposition does not exist then there is every likelihood that the trauma will rupture the organ in preference to displacing it.

I would divide trauma into two classes, that of intra-abdominal origin and extra-abdominal origin.

#### (a) Intra-abdominal

- 1 Straining due to constipation,
- 2 Tumors of adjacent viscera,
- 3 Colonic displacements,
- 4 Traction exerted by adjacent structures,
- 5 Renal tumors,
- 6 Renal calculi,

#### (b) Extra-abdominal

Sudden direct violence—

- (a) Blow
- (b) Strains
- (c) Falls,

Gradual,

- 3 Occupational anything which may cause continuous or excessive action of the iliopectus muscle

#### OPERATION

The essentials of the operation are

- 1 Restoration of the kidney to its normal anatomical position and relationship

Re-establishment to its normal mathematical and anatomical position, therefore restoration of its normal line of gravity, therefore less

encouragement for it to assume an abnormal position

3 Restoration of and fixation to its normal position by a method in which the normal intrarenal and extrarenal movements are neither modified nor prohibited

4 No interference with the kidney tissue.

5 Restoration of the renal capsule to its normal relationship to the kidney when the sutures are tied

6 All sutures employed in the fixation must be associated with structures which are in normal relationship with the organs and move normally with it

7 Any procedure employed must fix the superior renal pole in its normal position and the renal vessels seen to be at a right angle with the aorta and inferior vena cava respectively

The object of the practice of any operative procedure is to restore the abnormal part or organ to its normal position and condition. In any candidate for surgical interference the pathological conditions which exist present indications for operative interference which indications may be absolute or relative and the same may be said of contra-indications

In the case of abnormal mobility of the kidney the indications for operation may be divided into the primary and secondary or absolute and relative.

Primary indications are

- 1 Pain
- 2 Tenderness
- 3 Enlargement,
- 4 Fixation of the kidney in an abnormal position,

- 5 Rotation of the kidney
- 6 Intestinal obstruction,
- 7 Hydronephrosis,

Secondary indications are

- 1 Nervousness,
- 2 Digestive disturbance,
- 3 Intermittent pain,
- 4 Recurrent pain
- 5 Occasional discomfort
- 6 Gynecological reasons—
  - (a) Dyspareunia,
  - (b) Dysmenorrhea
  - (c) Metrorrhagia,

7 Marriage

8 Athletics,

9 Travel

Dr E. L. Keyes has written an excellent paper on the management of calculi in the solitary kidney but no mention is made in that paper or in any other publication which I have read, regard

ing the many cases of abnormal renal mobility in the kidney bed.

Recently I was asked to review one in which the left kidney had been moved some three years or so. The patient is far from well and the right kidney was enlarged, mobile and tender. In addition to her renal symptoms she was impeded in all her life and there was very pronounced general extreme atrophy. Reckoning that the operative danger was increased considerably on account of the absence of the left kidney, I decided to let her ride with her as proposed, accepted and was highly pleased with only very slight excessive per-operative and immediate post-operative. Therefore, I should not regret the decision of regard to the degree of the operative bed as a counter-indication to operation, but it must be remembered that should a renal tragedy occur, such as tearing of the kidney substance, with uncontrollable hemorrhage or tearing of the vessel themselves, then a fatal result is not definitely assured.

*Preparation of patient.* I have always decided to have the patient resting in bed for 48 hours previous to operation if at all possible. During this time the patient's general condition should be carefully examined and the total quantity of urine passed in 24 hours ascertained. The operative area is thoroughly washed with soap and water, cleansed by turpentine and then with spirit and finally by a 20 carbolic carbolase is applied but no gutter placed as this is never used.

This dressing is changed every 12 hours, and 2 hours before operation it is finally changed for a complete ring out of 1-2 carbolic solution which is applied and which is removed on the table when the area is finally swabbed with spirit. During this time the bowels are emptied by the use of purgative and an enema. The diet is liberal and nourishing and of a variety which is easily digested. No solid food is given for 6 hours at least prior to operation. Half an hour prior to operation a quarter of a grain of morphia is given and a two hundredth grain of atropine.

In the early operations the large curved sharp pointed needle of Doyen was used, which served the purpose well but I always felt that considerable damage might be caused by it. I therefore decided to design the needle which I now in variably use, and which is now described (fig. 5).

#### TECHNIQUE

This is most conveniently described in stages.  
*First stage.* At least 48, probably 72 hours should elapse between the admission of the patient and the performance of the operation and



Fig. 5. Transpiral nephropexy needle.

should not be a period of any further undiscovered constitutional condition present itself the operation must be delayed until matters are settled. The pre-operative period is to be occupied by rest, the amount of urine voided in 24 hours ascertained and the alimentary canal cleared and dressed in the usual manner.

*Second stage.* The anaesthetic is invariably employed by me as chloroform. I am quite aware that it is not the popular anaesthetic of today, but I have never had any reason to be dissatisfied with it and I am still a firm believer in the virus.

Such were so fully and perfectly expressed by my distinguished teacher, the late Professor Sir William Macewen. He and the staff administered by the ordinary simple open method and seldom has any difficulty been experienced. The patient is placed upon the operating table, lying flat on the back with the lumbar air pad in position ready for inflation. And then being completely the patient is turned upon the side opposite to the one being operated upon, the thighs flexed upon the abdomen, and a sand bag placed against the shoulder blades. By this means they are steadied in the desired position for operation. The inflation of the lumbar pad increases the costovertebral angle.

Four towels wall off the operative area and over them is placed a large sheet with an opening large enough to permit of the operation being performed.

*Third stage.* The line of incision is transverse and runs from the anterior border of the erector spinae directly forward  $\frac{1}{2}$  inch below the twelfth rib for a distance of from 3 to 6 inches, according to the size of the patient. With the first stroke of the knife skin and subcutaneous tissues are incised. The deeper tissues are now exposed and the fibers of the latissimus dorsi muscle are now recognized. In many instances they may be separated and the posterior border of the external oblique muscle is reached which is usually displaced forward.

As the result of the foregoing manipulation a quadrilateral space is formed bounded posteriorly by the anterior border of the erector spinae and quadratus lumborum muscle anteriorly by

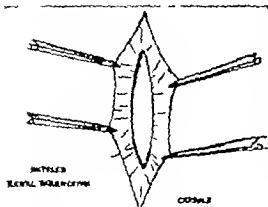


Fig. 4. The capsule of the kidney split and the renal cortex exposed.

the posterior border of the external oblique muscle and superiorly by the inferior border of the twelfth rib and inferiorly by the iliac crest. The floor is formed by the internal oblique and the lumbar aponeurosis. In this space will frequently be observed the twelfth dorsal nerve and sometimes the iliohypogastric nerve. They are if at all possible, carefully avoided.

The lumbar aponeurosis is divided transversely and also any of the fibers of the internal oblique if separation is found difficult. The lumbar fat and perirenal tissues are now freely exposed and the position of the kidney determined.

**Fourth stage.** During the previous stages of the operation the lumbar air pad has been gradually inflated, and the inflation is continued until the kidney makes its appearance in the depths of the wound. The kidney is steadied by being firmly grasped in the hand, if possible, and also by pressure forceps grasping the perirenal fat.

As a rule I do not deliver the kidney on to the surface of the wound as I find I can, by means of steadying it in the manner described, clear its convex surface and incise the capsule with ease (Fig. 6).

The organ has now been carefully examined and no tumors, cysts or stones found, the convex surface is now cleared of all perirenal fat, if such should be present. I do not clear the perirenal vessels to any greater extent than is necessary. Clearance having been effected, the capsule is now incised from the superior to the inferior pole. In the majority of cases the capsule can be easily incised without involving the renal substance but, if any difficulty is experienced, the incision can be commenced at the lower pole and continued up-

ward. A pair of blunt pointed dressing forceps is used so as to raise the capsule from the cortex but as a rule this is entirely unnecessary.

I have found the capsule separator of great help in many cases and I now invariably employ it, as it is a sure prevention against injury to the renal cortex. The instrument has no sharp bends, it is completely rounded and blunt pointed, therefore it cannot injure the renal tissue. After completion of the incision the edges of the incision are grasped by pressure forceps and the handle of the knife or a blunt director separates the capsule on either side of the incision for a quarter of an inch so that from  $\frac{1}{2}$  to 1 inch of cortex is exposed, the object being to produce adhesions between it and the surrounding tissues when the retention sutures are tied (Fig. 7).

Seven sutures are now introduced. Most surgeons use silk or gut. I use nothing but No. 3 catgut, each suture being one foot in length. The superior suture is first introduced at the superior extremity of the split capsule. The suture is introduced so that a small area of capsule is included round which two turns of the suture are made but is not tied because I believe it is unnecessary. Further if the knot should be too tightly tied there is a possibility of a localized area of necrosis developing and the purpose for which the suture was utilized is defeated.

The lateral sutures, which are of the mattress variety are introduced three on each side, 1 inch apart.

**Fifth stage.** The first suture to be dealt with is that of the superior pole. All sutures having been introduced, the superior ones are taken and threaded into the eyes of the renal needle which, when operating on the right side is taken in the right hand. If the kidney has been delivered on to the surface of the wound it is now replaced into the abdominal cavity, the inferior pole being replaced first, and the left hand of the operator is introduced with the palmar surface approximated to the internal surface of the thoracic wall. The needle is guided between the second and the third fingers to the tenth intercostal space and at the junction of its middle and posterior thirds the needle is made to perforate the space and its point appears beneath the subcutaneous tissues. A touch with the knife and the suture arches on the exterior and are then withdrawn from the needle. The delivery of the point of the needle on the external surface of the thoracic wall is accomplished with the greatest ease by simply separating and moving the fascial planes once the point is in the intercostal space and depressing the handle. The needle is now withdrawn and the

ends of the superior sutures held by an assistant who has secured them by pressure forceps. The lateral sutures are now threaded on to a round needle and left untied, and this suture is made to transfix all the tissues up to the superficial layer of the subcutaneous tissues, the skin edge being gently retracted. They are passed so that when tied they are at an angle of 45 degrees with the renal capsule. The anterior sutures are, as a rule, first placed in position. After all have been passed, the superior pole suture ends are threaded on to a round needle and stitched into the subcutaneous tissue and securely knotted. A single continuous catgut suture of the skin wound completely closes the wound in the subcutaneous tissues and the skin.

The lateral sutures are now tied and the kidney is thus secured in its normal position. It will be observed that no suture is tied outside the wound, which, on the completion of the capsular anchoring and the approximation of the muscular and fascial planes, can be completely closed.

The lumbar air pad is now gradually deflated and the muscular and fascial planes are closed by interrupted sutures. The skin, by interrupted cutaneous or subcutaneous sutures. Very often an anchor dressing is applied, which is more comfortable than a collodion dressing. A firm pad of cotton wool is applied to the abdomen and a bandage applied.

*Sixth stage* Immediately on the completion of the operation, 0.5 cubic centimeter of pituitrin is given and repeated once every hour for 6 hours, and a rectal saline composed as follows:

Glucose	½ ounce
Aspirin	20 grains
Potassium bromide	30 grains
Saline	10 ounces

is given and repeated in 6 hours if necessary. The patient is placed lying flat on the back for the first 24 hours. They may, if they will, lie on the side operated on, but not on the sound side.

The morning following the operation a flatus enema is given which is repeated once every 24 hours until the bowels act naturally. Commencing 24 hours after operation 1 grain of calomel is given every 8 hours until the bowels move. As a rule this happens not later than the third day.

This treatment has given very satisfactory results, in fact, many of the patients have hardly experienced any postoperative discomfort. Approximately 20 per cent have in addition required one hypodermic of ¼ grain of morphia, but as a rule it is neither requested nor given. When morphia is given it is dissolved in a 25 per cent solution of magnesium sulphate. By this method its

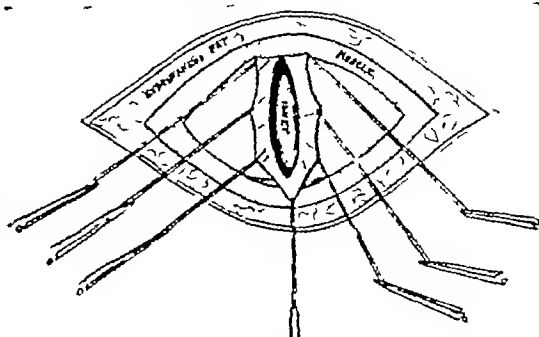


Fig. 7 The renal cortex exposed and sutures in position in renal capsule

efficiency is much enhanced and the possible ill effects are in most cases entirely obviated (synergistic analgesia).

*Seventh stage* At the end of the eighth post-operative day the wound is inspected, the anchor dressing removed, and the line of incision sealed with collodion. The abdominal pad of cotton wool is replaced and bandaged firmly. A course of massage is now commenced, the muscles of the anterior abdominal wall being first treated. After the first 3 days the whole body is massaged. The advantage of this treatment is that the muscle tone of the abdominal muscles is largely restored, the treatment in almost every case fatiguing the patient just sufficient to induce natural restful sleep.

Rest in bed is given for 21 to 28 days, after which time has elapsed they are allowed up for longer intervals daily. By the end of the sixth postoperative week they are, as a rule, fully restored to their usual habits.

Belts, trusses, or supports are as a rule not advised. If the operation has been successfully performed, they are unnecessary. They serve only to remind the patient of an unhappy past, hamper the action of the muscles, and maintain the loss of tone, and are a source of general discomfort and discouragement to the patient. If any sense of weakness is felt, which is unusual especially when the transverse incision has been employed, they may wear an ordinary 6 inch bandage or a woollen body belt, but the majority are only too glad to dispense finally with any apparatus they may have worn prior to operation.

#### RESULTS

The final decision as to the efficiency of any method of treatment is based upon results. Results are observed more promptly and definitely in the wake of surgical intervention than in any

other form of treatment. The success or failure, partial or complete of any form of surgical procedure is most accurately assessed by determining the number of patients who have been submitted to operation and the percentage of which as the result of such treatment, have been able to resume their usual mode of life or occupation. Further it is assessed by the length of time required to obtain that more or less perfect result, which infers that they do not require to restrict themselves either socially commercially or athletically and that they do not require to wear any form of artificial support. A patient who fulfills these conditions can be justifiably classified as a cure.

The 40 patients forming the subject matter of the present paper are classified as follows: 39 can be held to have fulfilled these conditions the last case may but it is at present too early to pronounce final judgment.

In assessing operative results, the following factors have to be considered:

1. Condition of the scar as regards

Appearance  
Sensibility  
Integrity

- a. Presence of keloid,
- b. hernia,
- c. deficient muscular action,
- d. contraction.

Position of replaced kidney

3. Restoration of normal function of replaced kidney and therefore disappearance of renal abnormalities which may have been present prior to operation.

4. Disappearance of all constitutional symptoms which were present prior to operation.

To place a true value on these results a fixed period of observation is essential. Many of the patients operated on have been observed for periods of time varying up to 9 years from the date of the operation but as a working rule I might be said that any case in which the organ remains in its normal position, and in which there is no recurrence of any of the symptoms for a period of 5 years from the date of operation may be classified as a permanent cure.

All the patients in the present group have been examined since the operation and the result to date is all that could be desired. In first case operation was done in 1904 and, while I have not seen patient personally for some years her medical attendant has informed me at this date that she has remained perfectly well, has borne several children, and has not had the slightest recurrence of symptoms since her operation.

The remaining patients have all so far complied with the requirements laid down in the first part of this section. Several patients in whom the nervous symptoms were the most prominent clinical factors have reported complete recovery and now lead normal lives.

To date so far as I know there has been no recurrence of the condition or of the symptoms, and no postoperative pain or discomfort. The fact is substantial proof that the laws and rules of physiology have been surgically correctly interpreted. That the operative procedures employed have not only restored the kidney to its normal anatomical position, but they have also been successful in replacing it in that position in a condition whereby it is enabled to resume its normal functions unfettered by any artificial restrictions and with its anatomical surroundings unchanged. That it is in that condition post-operatively, I believe, sound proof of the correctness of the principles upon which the operation is founded and the scientific accuracy of the operative technique which has been, and is, being employed.

#### CONCLUSIONS

The only description of this operation which I have seen is in Maynard's *Practice and Problems of Abdominal Surgery* and in that article the original technique is described in detail.

The present investigation has confirmed the original principle set down by its author, namely, that to be successful the whole convex border of the organ must be fixed, and especially the superior pole. So far as I know this is the only operation which fulfills that requirement.

While there is no doubt that abnormal renal mobility does occur in the male it is questionable if it ever occurs to the same marked degree or so frequently as it does in the female. The view advanced to explain this sex peculiarity may ultimately be found to be the one if not the only principal cause of true renal mobility and that true renal mobility is practically confined to the female.

While many well known surgeons are adverse at this present date to employ general anesthesia as a diagnostic aid, I submit that in at least per cent of my cases a diagnosis could not have been arrived at without its employment. By its use complete muscular relaxation is obtained, the various abdominal viscera can be palpated through the abdominal wall and any vascularity of support of which is directly or indirectly in any way deficient can be displaced from its normal position in a manner and to an extent impossible by any other diagnostic procedure.

Radiography and pyelography are useful, but radiography with the present technique is unreliable. I have stated that to date I have not employed pyelography as a diagnostic aid, my main reason being that one of the many recognized contra-indications to the employment of that method is almost constantly present, namely a marked supersensitive patient, and there are others which, in my opinion, outweigh any advantage which the method may possess as a diagnostic aid in this particular condition. There is, however, one condition in which it is of real value and that is the ectopic kidney. It certainly places the diagnosis of that condition beyond doubt.

During the progress of this investigation, a case of solitary kidney was met with. No precedent could be found indicating that the operation had been previously performed in such a condition, as has been stated. After fully considering all the possibilities, it was decided to perform the operation, as it is held that the operation in no way interfered with the actual kidney substance, and therefore is very unlikely to modify the renal function. The result has justified the theory, and so far as I can determine no reluctance need be shown in performing the operation which in this case produced the desired effect.

The fundamental principle remains unchanged. All investigations to date have gone to prove its scientific accuracy, but the method of accomplishing the operation has been modified to a certain degree. The needle originally used served its purpose but the instrument now employed is believed to possess distinct advantages, mainly that it is unbreakable, its curve is anatomically

correct, and, being blunt it can do no damage, therefore concealed hemorrhage or severe damage to the pleura or lung is effectively guarded against.

The transverse incision possesses the same advantage here as elsewhere and by its use not the slightest pulmonary embarrassment or complication has ever been experienced.

It has not been found necessary to deliver the kidney on the surface of the wound and by refraining from this procedure surgical shock of any degree has seldom been observed. The use of catgut has obviated the removal of stitches and allowed immediate and permanent postoperative closure of the wound which is very desirable.

The success of the operation has been shown by the ease and safety by which it can be performed, but the conclusive proof of its justification is demonstrated by the disappearance permanently of all signs and symptoms and the absence of recurrence, and its entire safety by the absence to date, of mortality. That the sympathetic can, and does, exert such a powerful influence over the patient is clearly shown by the disappearance after operation of all nervous symptoms.

To my late friend and Chief Dr. W. D. Macfarlane, I desire to record my undying gratitude as without his help, guidance, and encouragement at all times this work, such as it is, would not have been completed. To my friends Drs. Reid, Waddell, and Wilson for their assistance at all times I am truly grateful. Lastly to Mr. Boot for the beautiful diagrams I gratefully offer my most sincere thanks.

As the result of Maylard's pioneer work an operative procedure has been placed in our hands which to date has proved mortality free and by its results proved to be scientifically sound. By its use a certain proportion of the community has been converted from a life of chronic invalidism to a sphere of usefulness and social activity and for whom, prior to the operation, life held no joy.

## CHONDROSARCOMA

## THE RELATION OF STRUCTURE AND LOCATION TO THE CLINICAL COURSE

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**A**MONG the cases of bone sarcoma which have been treated during the past 5 years in the Graz Surgical Clinic, 9 cartilaginous structures were found. These have been verified pathologically and even though 2 were so far advanced at the time the patients entered the clinic that they presented more of a pathological than a clinical picture the cases are of value in a consideration of the prognosis and treatment of the condition. Although the histological structure in 5 of these tumors is such as to allow of inclusion with the chondrosarcoma, other factors would place them in the group of relatively benign chondroma. They are discussed here with the sarcomas, however because of the histological picture, which may be the same in the clinically benign form as in those cases in which clinical and X-ray examinations demonstrate a pathological invasion. They are included also because the course of chondrosarcoma of the small bones of the hand and foot is somewhat uncertain, the outcome depending on whether or not treatment has been given, and, if given, whether curettage has been complete. The 4 remaining cases contribute data as to the results in attempts to effect cures in outspoken malignant chondrosarcoma of bone. The results in these 4 cases may be considered in the light of (1) the histological structure, which permits one to judge, on the basis of statistics as to prognosis (2) the anatomical location—an important factor determining not only the surgical accessibility of the growth but also the association of the growth with numerous connective tissue and cartilaginous structures, the presence of which in joints provides the embryological soil from which these growths are believed to arise, just as they arise from the soil of later cartilaginous metaplasia, as in the sternum and (3) the time after operation before recurrence, the variability and uncertainty of which, somewhat paradoxically is the surest criterion as to prognosis.

A review of the records of such tumors from the files of a large surgical institution which deals chiefly with the diagnosis of malignant conditions and the most effective treatment of them, discloses a typical clinical picture. The value of case report depends on the extent and detail given as to the clinical, radiological, and pathological

examinations, so that conclusions here given depend on the evidence shown in the records and are based on the extensive knowledge of bone tumors that has accumulated in recent years.

The compilation of the American Registry of Bone Sarcoma has done much to clarify the diagnosis of such tumors. The extensive files of the Registry with its complete records of examinations in the cases included in the Registry lend authority to its statistics. From the classification of the Registry Geschickter and Copeland have evolved not only a histological picture but a description based on the embryological origin of the tumors and their genetic composition. In this paper, therefore, no attempt will be made to discuss the subject of chondrosarcoma in general, but we shall endeavor rather to discuss several cases in the light of what is already known. Conclusions are drawn chiefly from these. A summary of the histological relationships and their significance, factors in prognosis, indications for and the effect of treatment is presented with each case.

**CASE.** The patient was a laborer 40 years of age 4 years before entry he had squarred the fifth finger of the right hand. The swelling did not entirely subside, but gradually assumed firm character. Patient thought that this might be due to his habit of carrying bottles with the finger. Examination showed a half-inch sized tumor of firm consistency in the distal aspect of the middle phalanx, limiting motion. X-ray report: "Cystic expansion of the middle phalanx by a central bean sized area of resorption, with widened borders, that involves the proximal two thirds of the bone shaft—a chronic inflammatory affection of bone, probably tuberculous."—Prof. Leeb. Curettage for blower demonstrated bone cyst, the relations, blackish gray content of which showed under the microscope "sarcomatous tissue" with typical star shaped cells as well as remnants of bone tissue attached by osteoclasts, in addition to osteoid borders on the bone tissue—myxoma with bone destruction.—Prof. Bentske (Fig. 1) The specimen was described by Prof. Carl Sternberg as myxosarcoma, originating either in joint tissue or in bone. (Prof. Sternberg's comment: that the tumor may have originated either in joint tissue or in bone is noteworthy.) Intraarticular of the finger as performed through the carpo-phalangeal joint. Eighteen months following discharge, the patient showed no local recurrence or lung metastases.

This case is an example of phalangeal chondrosarcoma, histologically malignant but clinically benign particularly in the light of operative curability following early and complete removal in the absence of similar structures in other bones.

The giant cells may here be regarded as secondary agents in the destruction of bone by the mucinous tissue, but their appearance and location in the section (Fig 1) suggest a common origin for the giant cells and for the myxomatous tissue containing the giant cells. This view is supported by the fact that the skeletal location of chondrosarcoma and benign giant cell tumor closely corresponds.

**CASE 2** A laborer, 19 years of age, had noticed a gradual enlargement of the small toe of the right foot during the course of a year. He had had no antecedent infection or injury. Examination revealed a resistant, indurated swelling of the small toe, the size of a hen's egg. Amputation of the toe with complete removal of the tumor was done. Pathological diagnosis: "Terminal phalanx completely replaced by a plum sized lobular tumor mass of cartilaginous consistency, surrounded by a capsule. Microscopically composed of nodules, divided by connective tissue septa and composed partly of fibrillar and hyaline intercellular substance, and of cells which are in part similar to cartilage and encapsulated, and again are of spindle shape and of varying size. The cells are present in greater numbers than in normal cartilage. The tumor is sharply separated on all sides from surrounding fat and connective tissue by a completely intact capsule, and approaches in no place the edge of the incision—chondrosarcoma." Postoperative radiation was carried out for a month. Attempt to trace patient 4 years after operation was unsuccessful.

Unfortunately, the slide was not preserved. The occurrence in a phalanx and the sharp, though fibrous, encapsulation, suggest an enchondroma. But here the transition of cells to cartilage tissue seems to occur without a myxomatous medium, although the cartilage cells present are nevertheless of an embryonic type. The tumor reached a comparatively large size in the short time of a year, and, as will be discussed later, this rapid growth corresponds to the absence, or small amount, of myxomatous tissue. Whether a typical phalangeal chondromyxoma existed before the assumption of rapid growth can not be determined. Of further interest is the total destruction of the surrounding capsule of cortical bone.

**CASE 3** A boy, aged 14 years, had noted, 3 years before entry, that a small stationary tumor, which had been present for an indefinite time on the back of the left hand, began to grow. The growth made the use of the hand painful. The onset of increase in size was not connected with injury, as far as patient remembered. Examination disclosed a hard, nut sized tumor in firm connection with the second metacarpal bone. X ray film (Fig 2) "Aspects of a chondromatous degeneration of the bones of the hand with cartilaginous exostoses and endostoses. The largest exostosis arises from the lateral border of the shaft of the second metacarpal. The cartilaginous exostosis is about the size of a plum, has an uneven border, and indents the shaft of the neighboring third metacarpal from the palmar aspect. The upper end of this growth is not sharply defined so that operative removal seemed indicated to circumvent a possible malignant degeneration of this part. In the proximal phalanges of the third and fourth fingers are transparent bean sized areas, such as may be produced by en-

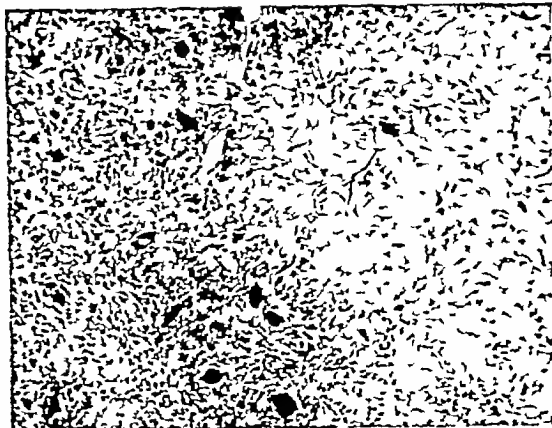


Fig 1 Myxoma with bone destruction, Case 1

chondromas. The bone shafts are expanded and broadened by one third of the normal diameter. Foot bones are negative"—Prof. Leeb. A glistening, nodular cartilaginous tumor, encased, except for the upper tip, in a thin, grayish-white capsule of the consistency of shrimp shell, was removed by chiseling through this attachment to the second metacarpal and curetting out the entire mass (Prof. Walzel). Postoperative X ray picture showed small scattered bone splinters in the operative wound bed. The histological section was that of a typical chondroma (Fig 3).

This case occupies a position midway between the first two. It resembles the first in that its structure is myxomatous and is divided into lobules by connective tissue septa, and in that it is sharply circumscribed by a bony capsule. It resembles the second in its tendency to penetrate and destroy the capsule at one point. It is not characteristic of a typical cartilaginous exostosis, or osteochondroma, because of the overwhelming predominance of myxomatous cartilage and the complete bony encapsulation (except for the one point of penetration), as well as its diaphyseal location. It is reasonable to assume here that the areas appearing as enchondromas in the roentgenogram possessed the same histological structure as did the peripheral growth which was removed at operation. The relation of the peripheral growth to its capsule was the same as that of a typical central chondroma which grows against, and bursts through, its bony confines. It is illustrative of the course of a growing phalangeal chondromyxosarcoma unchecked by operative intervention, and it also is illustrative of the possible future course of associated phalangeal enchondromas. Although the patient lacked the gross stigmata of Ljrenfred's hereditary chondrodysplasia, often found as the background of multiple chondromatosis, the broadening of the phalangeal metaphyses is suggestive of this asso-





Fig. 2. Kosteren, rare Case 3.

culation. That the operative removal was not radical allows room for the assumption that this cortical chondroma will recur. That a similar histological appearance is characteristic of benign phalangeal chondroma myxoma contained in a cortical shell brings out not only the fundamental similarity of chondroma and cartilaginous exostosis, but the justification for the term cortical chondroma for this tumor. It strengthens the view that the benignity of the central phalangeal chondroma is at least in part determined by the cortical shell, which, in the case of the myxoma arising in this exostosis, is not complete enough to check the mechanical tendency of this type of tissue.

**CASE 3.** A housewife, aged 30 years. Her only previous illness, pleurisy, years before admission. Inconstant pains were not felt in the sternum. Months previous to entry five months swelling over the sternum, slowly increasing. She had been noticed to be hard on small light pins. Her right side when working. Examination revealed firm solid somewhat lumpy tender swelling in the middle of sternum. The skin over the tumor was of normal texture and color without attachment to the bone. X-ray report. Sternum differentiated only faintly because of high grade demineralization of the bony center. Fluctuating under the manubrium. In early months scattered areas of tracing spines. Over and above



Fig. 3. Typical chondroma, Case 3.

or of tuberculous. The lowest portion had normal cut separation. (Postoperatively, roentgenograms of the sternum gave the same findings.) Biopsy the specimen was probably from grade containing crumbly pieces of loose the posterior sternum. All was reduced to paper thickness. At autopsy report. Blood and numerous irregularly formed and growing cartilage cells in adjoining clusters—chondroma. Sternum resection. As done April 5, 1933 (Prof. W. Br.)

Incision. As made over the manubrium sterni about 15 cm. Each the size of goose egg. Division of cartilaginous ribs—second, third, fourth, and fifth—from the left. The left sternum margin was lifted and freed from its adhesion.

At the left pleura and pericardium. The tumor positioned posteriorly, but did not infiltrate the pleura, the corresponding costal cartilages on the right were divided and the sternum removed by chisel just beneath the upper border of the manubrium. Microscopic examination of the specimen showed "Cartilage tissue. It was normally widened cartilage on ribs and densely laterofiber substance. Some areas contained many cells, the cartilage tissue was infiltrated the bone and exhibited necrosis and hemorrhage. Chondroma, with partial trabeculae of marrow." Prof. Becke (Fig. 4).

One month later two control X-ray pictures showed only the remainder of the normal sternum. Patient discharged as healed. May 6, 1933. Three months later another control showed only dark calcium deposit in the region of the resection. Six months following discharge the patient entered again because of first phase sternal growth. The upper end of the sternum. X-ray examination October 24, 1933, showed. Oblique view of sternum, body resected. Manubrium atrophic, with irregular contour and small area of bone destruction beneath the right sternoclavicular joint. Lung fluoroscopy.

Pyramidal shadow of soft tissue opacity in the periphery of the left lower lung field. October 25, 1933, as above resection. (Prof. W. Br.)—separation of sternal portion of pectoral muscle. The tumorous proliferation corresponded the right hand portion of the manubrium sterni. The right clavicle was divided at the junction of inner and middle thirds and of the right first and second ribs. Tumor breadth from their manubrial attachment. Devascularization of the left side of manubrium was done at junction with left clavicle and first and second ribs. Tumor was showed best at sternal tumor infiltration the lower control. X-ray examination confirmed removal of tumor. Lower and portion of clavicle well. Presence of residual shadow in the left lower lung field of soft tissue density having the appearance of tumor metastases, or

of confluent lobar pneumonia November 26 Patient was discharged as healed January 1, 1934, X ray examination revealed "Infiltration in the lower lobe of the left lung unchanged" Differential diagnosis lay between metastasis and organized remnants of the empyematous infiltration Fibrous induration of both lung hili Sternum and sternal third of right clavicle were absent Flecks of calcification arose from the medial border of the first rib Last control (May 8, 1934) showed a diminution in size of the opacity in the left lung field, which was then assumed to be the remainder of an interlobar pleurisy Patient received radiation therapy following each operation

The histological structure is again that of a chondroma, with transition to sarcoma The myxomatous tissue is scarce and irregularly formed The absence of evidence of a pre-existing tumor, and the fact that the recurrence bore the same microscopic appearance as the first tumor, speak in favor of a primary sarcoma On the other hand, it seems to have been central in origin, and this, with the location in the sternum and the age of the patient, suggest an enchondromatous origin However, it is questionable if an enchondroma can exist in such a location in a patient aged 40 years, and still remain benign If this tissue is histologically that of a central chondroma in its early stage of development, it belongs to the division of secondary chondrosarcoma, in which the malignant change occurs soon and rapidly, or it illustrates clinically what is more frequently seen under the microscope—the uncertainty of the character of the primary tumor and of the prognosis A further recurrence may almost be expected, although the patient is now without X-ray evidence of recurrence 8 months after the last operation<sup>1</sup>

CASE 5 Soldier, aged 25 years, was admitted to the clinic August 10, 1933 Three months previously he fell against a stone during an infantry maneuver, striking the upper portion of the left thigh, producing a bluish swelling that lasted a week, and severe pain that at first prevented walking The pain subsided somewhat, but since then persisted, radiating down toward the knee, at night especially severe He has limped since the accident Three months later an X-ray examination was made and the presence of an impacted fracture in the trochanter region on the upper border of what appeared to be a "myelogenic sarcoma" was reported On admission to the clinic the upper third of the femur was enlarged and tender Hip movements were not limited, but painful The first X ray picture (Fig 5a) bears the following description "Lemon sized area of transparency beginning in the upper third of the femur shaft extending to the trochanter region The bone is expanded to double its normal thickness at this point, about which periosteal apposition is present There is no break in the continuity of the bone The condition exhibits a slowly progressing central process of destruction

<sup>1</sup>The patient returned again in September, 1934 11 months after the last operation with a large recurrence in the operative scar eroding the proximal ends of the ribs and with lung metastases A particularly dense clouding of the left lower lung field confirms the impression that the infiltration seen during the preceding months was a pulmonary metastasis



Fig 4 Chondroma with partial transition to sarcoma, Case 4

with periosteal new bone formation on the border This circumstance speaks against a malignant tumor and may represent a benign, probably chronic, inflammatory area of destruction"—Prof Leb Curettage was done August 19, 1933, by Docent Susani exposure of the bone revealed a rough surface penetrated by cavities, within which there was gelatinous tissue Complete curettage of this tissue was done and removed, with pus from a large central cavity Patient was immobilized in a cast, and the wound healed after 2 months X ray treatment was given after operation Microscopic report from curettage "Network of hyaline connective tissue with calcium deposits, among which nests of cells were present, lying close together, with star shaped branching nuclei—chondrosarcoma"—Prof Korschegg This diagnosis was confirmed by Prof Sternberg X-ray findings a month following the operation "Distention of upper portion of femur shaft to double the normal size Central, irregular areas of destruction extended into the intertrochanteric region and at this point penetrated and destroyed the lateral cortex (operative defect) The medial cortex was thickened and strengthened through the newly formed periosteal apposition In the direction of the bone shaft, there was periosteal reaction with strong newly formed bone The expansion spoke for a slowly growing process of destruction The perforation of the lateral cortex would nevertheless speak for a malignant process Together with the marked periosteal reaction, the finding would not speak so much against a malignant tumor as in favor of relatively slow growth and benignity, This finding is given for giant cell tumor, osteochondrosarcoma, slowly growing hypernephroma metastasis, etc Evidence is that of a differentiated, slowly growing malignant tumor"—Prof Leb X ray pictures taken a month after this gave essentially the same result, except for a sharper circumscription of the transparent areas which were enclosed peripherally by a strong wall of periosteal bone Following discharge, X ray therapy was given

Patient returned 5 months later March 9 1934 with a hard tumor the size of a grapefruit in the region of the great trochanter this had appeared during the previous month and was associated with a renewal of radiating pains Hip motions were limited and painful, thigh and gluteal musculature atrophic X ray, March 10 showed regeneration of the cortex which had previously been destroyed by the curettage as well as two small bone defects on the lower border of the operative cavity (Fig 5b)—a lateral view

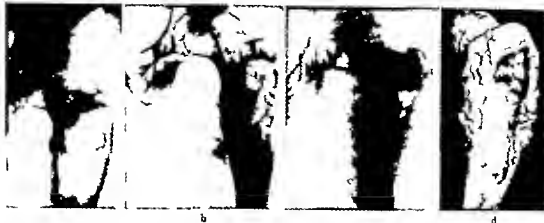


Fig. 3. a, First roentgenogram, Case 5. b, 7 months later. c, 10 months after b. d, photograph showing formation of spicules and perforations in the cortex.

showed further the sharp demarcation between shaft and intertrochanteric regions. Operation, March 6, 1934, by Docent Sessén, showed gelatinous tumor masses filling the bone cavity and extending into the musculature, where they were surrounded by firm, fibrous capsule. The tumor penetrated the remaining shell of bone in several places. Curettage was done and the bordering areas of sound bone were removed. Pathological report: "Dense connective tissue interspersed with serous and hemorrhage. Among these nests of spindle and star shaped branching cells in an intercellular substance which stained blue with Van Gieson. In addition, cavernous bone showed transition to reddish-staining homogeneous tissue to which numerous, large, irregular cells were applied. The bone trabeculae themselves showed extensive regressive changes—osteoid chondroid areas." (Fig. 6). Following this operation, radiation treatment as done. On April 30 radiograms of radium were completed in the granulating wound cavity for 8 hours, the cavity had been prepared for this supplementation by sewing the skin edges to the periosteal borders of the bone defect. X-ray examination, May 9, demonstrated a deeper destruction of the area of bone destruction (Fig. 7c). In the following 3 months 1 or three small wound recurrences

were removed by electrocoagulation, the pathological report of one showing patches of large pale, round and spindle shaped cells and many thin blood vessels, associated with pale blue staining tissue consisting of large round and star shaped cells, in the midst of which there are pale brown fibrillar ground substance. Not definite whether it is chondroma or chondrosarcoma. The last X-ray film, June 9 gives a deeper demonstration of the defect in the lateral portion of the neck of the femur than before. In the region of the lesser trochanter are short bone spicules arising from the periosteum and extending into the vicinity of the medial side of the lesser. These changes were demonstrable in the control picture taken 1 month before. The lungs showed no metastases.

(1) personal communication following the conclusion of this paper, Docent Sessén informed me that he had successfully performed an arthroplasty amputation of the involved femur and although the sarcoma had deeply infiltrated the medial musculature of the thigh, it had not extended above the level of the neck of the femur and the lungs had remained roentgenologically free of metastases.)

Figure 3d, is a photograph of the upper end of the resected femur following its necrosection, and shows the formation of spicules and perforations in the cortex.

In this case trauma may have lent growth impetus to a malignant tumor. The predominant chondromyxomatous structure, both histologically and roentgenologically, and the central location in the upper femur shaft, with the age of the patient, suggest an enchondroma or central chondromyxoma. That the symptoms associated with the injury fitted in with those present at the time a malignant tumor was found to exist—an interval of 3 months—fits on the impression that a direct traumatic insult occasioned the development of a sarcoma from a benign central chondroma. This provides a good example of the failure of vigorous X-ray and radium therapy to check such a growth, although apparently limiting its progress through the stimulation of calcification and new bone formation. Of interest is the recent formation of bone spicules on the medial side of the femur. Although from the standpoint of structure one might infer that the periosteum would be elevated only by the presence of malignant or inflammatory tissue, with the subsequent production of periosteal bone columns to support it, it is unusual to find periosteal spicule formation in association with a central, bone-destroying chondromyxosarcoma in the presence of a cortex roentgenologically intact. At operation, however, the myxomatous cartilage was found not only to have penetrated the cortex in a sieve like fashion, but to have infiltrated the surrounding soft parts. This finding provides a commentary not only on the size of cortical defects necessary to X-ray



Fig 6 Osteoid chondrosarcoma, Case 5



Fig 7 Chondroma with transition to chondrosarcoma

representation (2), but on the roentgenological translucency of the tumor itself. The reactive thickening of the surrounding bone tissue has been emphasized by Phemister, and there is little doubt that the advance of this reactive encapsulation was enhanced by the continued growth of the tumor as well as by the radiation. The intense X-ray and radium therapy makes it impossible to judge as to how much of the ossification present in the last microscopic sections was due to this therapy and how much to a more malignant tendency of the tumor. That the ossification is not purely of a reactive nature is shown by the presence of an osteoid matrix in the extensions of the tumor into the soft tissues (Fig 6).

**CASE 6** Man, aged 36 years, had noticed for  $2\frac{1}{2}$  years increasing pain in the left leg and sacral region,  $1\frac{1}{2}$  years, defective sphincter control,  $\frac{1}{2}$  year, impotence. Sensory and motor disturbance was present in distribution of the left sciatic nerve. X-ray examination January 3, 1933, revealed focal bone destruction in left half of the sacrum. Operation, January 14, 1933, by Prof. Walzel consisted, first, in the removal of the coccyx and lower segment of the sacrum thus revealing a coconut sized tumor on the inner surface of the sacrum, displacing the rectum inward. The tumor was not infiltrative, and possessed a nodular, dark gray capsule. An attempt to mobilize the tumor tore it, thus freeing friable gray masses of tissue. The tumor originated from the sacrum, the inner side of which it completely corroded. Prof. Walzel then curetted the bone and by blunt dissection removed the tumor except for some portions attached to the rectal wall and a portion above the sacral promontory which could not be reached. Pathological report: "Numerous, crumbly, nut sized pieces of cartilaginous tissue with numerous deeply situated cells, the capsules of which were not everywhere well developed. In these areas, the cells lay close together in a strongly basic staining ground substance—chondroma, with transition to chondrosarcoma."—Prof. Kosschegg (Fig 7). Prof. Sternberg, from the microscopic section alone, regarded this as a chondroma. An X-ray examination 2 months later showed only the operative defect, but 4 months after the operation there was a roentgenologically visible recurrence in the left

lateral mass of the sacrum, infiltrated by a number of transparent nut sized areas of irregular contour. Patient was discharged 2 months previous to this time with continuation of X-ray treatment, without pain and with restoration of sphincter function. Following discharge, the bladder and rectal function was gradually lost. A letter from the patient received 10 months after his discharge told of a huge recurrence and a cachectic condition.

This is a chondrosarcoma very similar to that of the upper femur in structure and course, but the location of which made it inaccessible to complete surgical removal. It is interesting from the standpoint of its chondromatous structure, its corresponding refractiveness to radiation, and its roentgenological translucency, permitting X-ray demonstration only of those parts of the tumor which were destroying bone.

**CASE 7** A tailor, aged 77 years, gave a history of "gout" in childhood, dislocation of the right hip 20 years before entry. There had been a gradual development of a coconut sized tumor on the inner surface of the right thigh during the course of 8 years, which, during a year before the increase in growth began, made its appearance as a very small, allegedly stationary, mass, associated with pain in this region. X-ray report September 22, 1933: "Extensive destruction of the horizontal ramus of the right pubic bone. Extending into the soft tissue from this area is a coarsely granular, flakily calcified tumor the calcium content of which disappears toward the periphery. This under portion can correspond to the rapidly growing sarcomatous part of the tumor. Lungs negative." Radiation was without effect, and the tumor grew until it seemed larger than the rest of the patient. A photograph taken prior to its maximal size development is shown in Figure 8. X-rays before death showed no evidence of osteitis deformans (Paget) in skull, vertebra, pelvis or tibia, or tumor formation in these bones or in the lungs apart from the local growth. Autopsy, December 20, 1933: Huge, partly necrotic, partly calcified tumor, occupying most of the right thigh, pelvis, and gluteal region, originating from the right horizontal ramus of the pubic bone, in its peripheral areas of gelatinous character. The pubic bone was the only one destroyed or invaded by the tumor. Histological report: "Tumor tissue crowded



Fig. 8 Photograph just prior to pressure development, Case 7

with cartilage like cells, some more, some less differentiated, in places necrotic, in others bearing the structure of an osteoid chondrosarcoma peripheral portion, myxomatous cores (Figs. 9, 10.)

The rarity of bone sarcoma after the age of 50 years and the increasing ratio of bone sarcoma to Paget's disease after this age (4, 18) with the greater frequency of a combination of the two with increasing age, gives note to this case in view of the age of the patient (77 years) and in view of the absence of osteitis deformans. The fact that the patient was a tailor and that the characteristically sitting posture was maintained on and off for over half a century may have been an inciting factor in the tumor growth arising at the origin of the sartorius muscle but it does not call for too serious attention. The apparently uniform growth of the tumor during 8 years is unusual, however this suggests a primarily chondromatous growth, and taken together with the fact that it was bone destructive only at its point of origin, where the type of resisting tissue was of more consequence in checking a relatively benign growth than an eroding tumor of higher malignancy is significant. It is also worthy of note that, although this sarcoma extended along practically the entire length of the femur it produced only a mechanical distortion of that bone. The patient described a small tumor at the original site of this growth which disappeared 3 months after the reposition of the disarticulation of the right hip, this accident occurring 2 years before the onset of the main growth. This may have been a hematoma following an anterior dislocation and suggests the origin of this sarcoma in that type of traumatic osteoma which has been known to follow such a dislocation (27).

CASE 8. Woman aged 48 years was struck on left side of chest 3 years previously. Since then this area has been

painful and sensitive. Three years before entry there appeared hard, slowly growing nodule. Three months before admission, lesion shed tumor and piece of rib were removed in an outlying hospital (report from this operation: "no definite sign of malignancy"). There was recurrence in the operable wound 2 weeks later. Two months after that the growth occurred when it had reached its former size. Histological examination at this time "osteoid cores. A week later there is recurrence in the wound. Clinic entry tumor since removed 6 weeks before now, grown to orange size. Biopsy: "Tumor consists here and there of thickly distributed cells with sort of capsule suggestive of cartilage cells. Among these are delicate collagen fibers, occasionally the cells are grown in thicker bands in other places, there is predominance of fibers and bone trabeculae, also microscopic areas with star shaped cells, much necrosis—osteochondromyxosarcoma. X ray examination shows stated only diffusely opaque tumor arising from the wall of the thorax. There was progressive growth of the tumor in spite of anterior resection. The patient became more and more as removed from the hospital by relatives.

The location, course, and reported structure of this tumor with the age of the patient, imply a sarcoma arising on the base of an osteochondroma or chondroma. This is suggested by the initial slow growth of the tumor and the result of the outside pathological examination speaking against malignancy. Whereas the tumor at first required 3 years to reach the size of a lemon, this size was regained 2 months after the first operation, and less than 6 weeks after the second. Although spontaneous malignant change can lead to a sudden increase in size, this bears the implication that operable interference stood in causal relationship to the further malignant course of the sarcoma. The report of the microscopic section (the slide itself was not preserved) does not, in itself allow a distinction to be drawn between primary and secondary forms of chondromyxosarcoma.

CASE 9. Woman aged 45 years, had hard tumor on the lower gum which she had noticed for 9 months, at which time it had steadily increased in size and several erythematous teeth had fallen out. Examination showed a whitish sized rounded tumor next to the dental margin in the lower anterior alveolar process—smooth reddish, lobular containing two loose teeth (Fig. 8-4 wk. after biopsy). Biopsy April 27, 1934. "Tumor merely surrounds the root of the embedded teeth covered by stratified epithelium and consists of nests of smaller and larger rounded spindle cells, which are separated by distinct intercellular substance. Among these cells are scattered giant cells and numerous small islands of cartilage, here and there the tumor invades and destroys the bone (Fig. 11). X ray pictures were taken April 28, 1934, and showed a bone-containing tumor in the central portion of the lower jaw. Originating from the alveolar border of the anterior teeth, an elevated mixed tumor shadow consisting of bone tissue and fleshy substance projects forward. The anterior all of the alveolar process is destroyed in the region of the chin (Fig. 12). Lung showed no evidence of tumor metastases. In the 6 weeks preceding operation and following the biopsy the tumor had tripled in size. Operation (Prof. W. J. Coffey) the



Fig 9

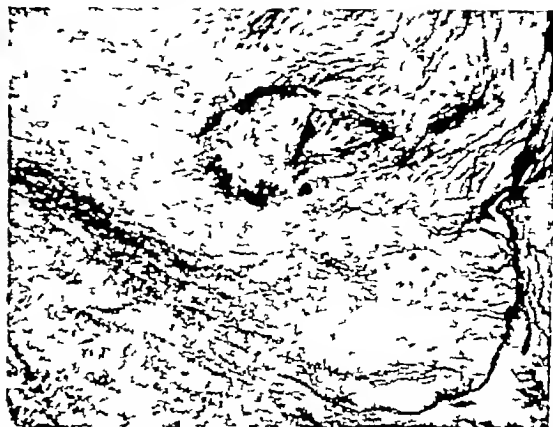


Fig 10

Figs 9, 10, 11 Photomicrographs, Case 7

tumor, the size of a billiard ball, was removed by chiseling about the broad pedicle arising from the gingival margin, the pedicle was coagulated. Pathological report from operation: "Firm, nodular tumor, glass-like cut surface covered with stratified squamous epithelium under which are large, round cells, closely placed, also polynuclear cells, as well as small, round, somewhat star shaped cells with jagged, indented nuclei. These cells pass over indistinctly into a pale, blue staining mass containing cartilage cells lying in large oval capsules, groundwork of delicate connective tissue—chondrosarcoma"—Prof. Korschegg (Fig 15). Subsequent roentgenogram showed only an operative defect at the previous site of the tumor extending almost to the under edge of the lower jaw without evidence of malignant change in the adjacent bone. Operation was followed by radiation.

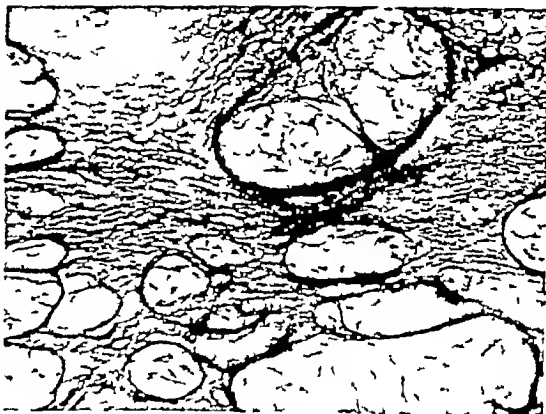


Fig 11

The presence of a primary chondrosarcoma is here suggested by (1) the rapid development of this tumor in a short time, (2) the evidently periosteal origin without a preceding chondroma or osteochondroma, (3) the bone formation extending into it at the base and periphery from connective tissue strands which give rise to direct and not to cartilaginous ossification, and (4) the absence of central involvement and presence of myxomatous tissue, although the histological structure in several parts is suggestive of a chondroblastic sarcoma. Its location is unusual, and to the eye raises the question of epulis. This tumor has just been operated on, a cure can hardly be expected. From the type of chondrosarcoma and its location, recurrence will more probably be in the form of lung metastases than at the site of the original growth.

#### RECAPITULATION

The bone tumors presented here fit into three divisions: enchondroma, and primary and secondary chondromyxosarcoma, according to the

criteria given by Geschickter and Copeland. Although they readily fall within the scope of such criteria, they exhibit variations in cartilaginous structure due in part to extensive growth or to treatment. They represent all stages in the evolution of atypical cartilage development from myxomatous tissue arising from precartilaginous connective tissue, to maturer encapsulated cells lying in a cartilaginous, calcified, or osteoid matrix, or accompanied by direct ossification from strands of embryonic connective tissue. But the predominantly cartilaginous structure allows these tumors to remain securely in the categories in which they are placed, although the occasional patches which show a tendency toward ultimate differentiation substantiate the basis of Kolodny's consideration of all malignant forms of tumors arising from "pre-osteoblastic" cells as osteogenic sarcoma. Enchondromata are only relatively benign, this benignity depends more on their surgical curability than on their histological structure or ulti-



Fig. Tumor protruding from lower jaw, Case 9.



Fig. 3 Photomicrograph, Case 9, biopsy specimen.

mate course when untreated. The great rarity of benign enchondromas of the long shaft bones suggests that the relative stationary nature of those found in the small bones of the extremities is dependent upon something more than the type of constituent cell. That even these may be looked upon with suspicion is justified by the malignant metamorphosis occasionally occurring after many years (20) by the attainment of a tremendous size, and by the occurrence of such cases as that reported by Castren, in which typical small enchondromas of four small bones of the hand were associated with a similar growth in the axillary lymph nodes of the corresponding arm. There are other instances of enchondromas having the pure, unvarying structure of the phalangeal myxoma, but, in a long shaft bone pursuing a recurrent metastatic course. The warnings of Blood good (5) with regard to the "pure myxoma" of the long shaft bones emphasize the dangerous nature of this type of tissue when it is not confined to the small bones of the extremities, although, as the 9 cases presented here suggest, the predominance of myxomatous tissue is associated with a relatively slow growth and one tending more to local recurrence than to early pulmonary metastases. One regards with greater complacency the osteomas and osteochondromas containing much bone and may infer from a comparison of the two that the inhibition and limitation of growth is in great measure dependent upon the bony capsule of the tumor. The stationary charac-

ter of the central phalangeal chondromas of Case 3. In contrast to the progressive increase in size of the associated cortical chondroma, the fact that a malignant change in an osteochondroma follows operation more often than if operation is not done, and the danger entailed by the spreading of gelatinous myxomatous tissue in an operative wound, contribute further to this belief. The peripheral chondromas of Cases 1 and 3 are the best examples of the restriction the histological report of the sarcomatous tumor in Case 8 leaves doubt as to the presence of much myxomatous tissue, but varying amounts of this were present in the 6 other cases which ran a less early controlled course, and in each of these 6 other cases there was no such confinement to a small space by a capsule of cortical bone.

In addition to this factor of confinement by a capsule of cortical bone, a second factor which seems associated with the malignancy of these growths is the greater differentiation of the cartilage cells, contradictory as this statement may seem. The cases in which growth was most rapid and in which there was a tendency toward early recurrence or quick destruction of the adjacent normal bone—those in the jaw, sternum, rib, coccyx, and toe (the last-mentioned an admitted exception)—demonstrate a relatively small amount of myxomatous tissue in contrast to the predominance of islands of highly cellular cartilage, in which the cells are relatively well encapsulated and embedded in a cartilaginous matrix. In these tumors are small areas of calcification and in some also areas of bone formed either by direct or by cartilaginous ossification. The opinion that the more highly differentiated cartilage cells grow more in the manner of a malignant growth than in that of less differentiated cells embedded in a



Fig 14. Roentgenogram, showing destructive process in region of chin, Case 9

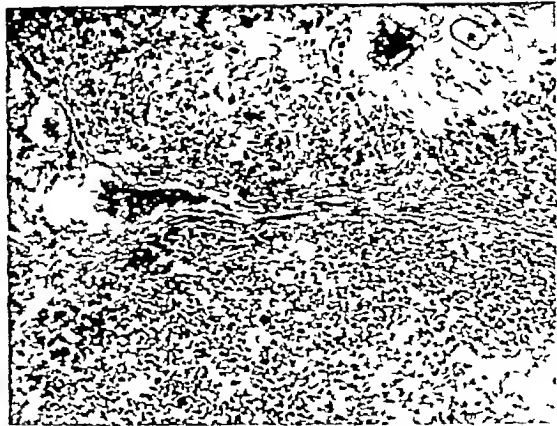


Fig 15 Photomicrograph, Case 9, from operation specimen

myxomatous matrix is derived more from the fact that there is a more active corrosion of the surrounding bone and rapid progress than from any reasoning from the standpoint of cell genesis. The best explanation is probably found in the view expressed by Leriche and Policard, namely, that the bony metaplasia in the neighborhood of an area of bone sarcoma results from destruction of normal bone and the liberation of its constituents by the sarcoma, which provide a matrix for the sarcomatous cells. Judged in this light, such differentiation is in reality a measure of the destructive progress of the younger myxomatous tissue rather than a mark of the malignancy of the cells which are surrounded by a cartilaginous or osteoid matrix. It is evident from the two microscopic sections of the chondrosarcoma of the lower jaw (Figs 13, 15) that a more mature cartilage cell developed during the period of growth acceleration at the expense of the patches of myxomatous tissue which were seen scattered in the material which was removed at an earlier date. Although this need not throw doubt on the more primitive nature of the young cells embedded in the undifferentiated matrix, it does indicate an inhibiting influence of this matrix on the young cells which are embedded in it.

The greater malignancy of the more highly differentiated chondrosarcomas need not conflict with the roentgenological and clinical evidence that large, localized cartilaginous tumors, such as that of the pubic bone in Case 7, containing large, flaky deposits of calcium and osteoid matrix, are more slowly growing and more benign than the infiltrating growths retaining an X-ray translucency. Such calcium deposits, which can be looked upon as secondary to diminished blood supply and

necrosis in a slowly growing tumor are to be distinguished from the shadows cast by cartilage and bone which arise through a primary, neoplastic formation of these elements from the cells which are growing malignantly in this type of sarcoma and which are the precursors of the bone and aberrant cartilage formed from them. At the same time, the "malignant differentiation" here referred to is more a property of the individual cells, it never attains the orderly structure of bone trabeculae and the relation to cartilage found in the roentgenologically more opaque tumors of an osteochondromatous type. Such secondary ossification is the metaplastic accompaniment of a primary cellular malignancy and arises from cells the differentiation of which follows more that of normal bone.

Nevertheless, the impression that myxomatous cartilage is less aggressive than are other maturer cartilage formations in chondrosarcomas is more easily reconciled with the viewpoint that such a gelatinous matrix represents a product of degeneration and not an early embryonic stage. This view is held by most European pathologists, and is reiterated by Prof. Carl Sternberg (36), he regards myxomatous tissue as one of several types of derivatives of embryonic connective tissue which may be present simultaneously with another type of derivative, cartilage, but does not represent an intermediate grade in the formation of the latter. Sections taken from different parts of the huge chondromyxosarcoma of the femur (Figs 9, 10, 11) suggest that there may be more than one sort of myxoma structure in cartilaginous growths. Circumscribed islands of dark nucleated cells with star shaped cytoplasmic processes embedded in a faintly staining mucinoid



whether it is to be successfully combated only by destruction or removal of adjacent tissues of which it is essentially a part.

The treatment of the cases presented here will be considered in the light of the factors just discussed. The 3 cases of phalangeal chondromatous growths were treated by amputation that of chondromyxoma of the finger phalanx remained healed after a year and a half that it will remain cured is hardly to be doubted. The large tumor of the toe in Case 3 grew rapidly and in the course of a year had completely destroyed its bony shell. The report of the microscopic section suggests an absence of myxomatous tissue and an irregularity of structure. Four years after operation, the patient could not be traced, but the complete fibrous encapsulation of the tumor within the toe is reasonable assurance that it has not recurred. The postoperative X-ray photograph of the meta-carpal chondroma showed bone splinters in the wound bed and an irregularity in the cortex from which the tumor took its origin. From the incomplete curettage of the cortex and the scattering of the fragments in the soft tissue a recurrence may be expected. This patient was operated on too recently to allow of judgment at present, but a recurrence arising from the same metacarpal bone should justify the removal of the entire bone at the next operation. Such cases are particularly adapted to operative removal. The malignant appearance of the cells from the chondrosarcoma of the toe was sufficient reason for postoperative radiation, and the effect of this form of therapy in stimulating defensive bone production recommends its application following incomplete removal of a chondroma.

Two cases were too advanced for surgical intervention—the massive sarcoma of the pubic bone, and that apparently originating in a rib and spreading into the thorax. In the former location and size contributed to a fatal prognosis, and in the latter the extent and probable presence of metastases.

The chondrosarcoma of the coccyx proved itself at operation to be incompletely accessible and from its further course refractive to radiation. The tumor of the body of the sternum seemed to have been totally removed at the first operation and without an intrusion into the malignant areas which might have freed tumor cells into surrounding tissue. Although it was circumscribed the tumor contained a variety of cells of cartilaginous origin, progressing to the point of osteoid tissue and exhibited irregular patches of bone destruction which showed none of the regularity of encapsulation of the chondromatous

type. Six months after operation there was a recurrence in the manubrium, which, in its turn, was subsequently removed. The manubrium and body of the sternum are not only parts of the same bone, but cartilaginous ossification is going on at the same time in both and although the recurrence in the manubrium may have existed microscopically at the time of the first resection, this again speaks for the removal of as much as possible of the genetically related tissue when the situation and extent allow a surgical procedure. If pulmonary metastases do not terminate this case which at the present time is clinically and roentgenologically free of tumor a recurrence in the associated costal cartilages is not unlikely (see footnote to Case 4.)

The inefficiency of curettage and radiation in its most direct form—radium implantation—is well illustrated by the case of central myxosarcoma in the upper femur metaphysis. It also shows the outspoken clinical malignancy of a tumor which was of a myxomatous type at the outset, and later on of mature bone forming cartilaginous tissue. The roentgenograms following X-ray and radium therapy (Figs. 5 b and c) show a striking increase in bone density and a sharp, ossified limitation of the primary tumor area. Though osteoid tissue and bone were present in the malignant cell groups in the surrounding tissue (Fig. 6) this was not enough to be visible in the X-ray pictures, even though this formation may at least have been accelerated by radiation (17). In view of the resistance of such cartilaginous new-growth to X-ray treatment, the benefit derived from this form of therapy seems to rest chiefly on its stimulation of reactive bone formation. Although bone sarcomas of the upper end of the femur are regarded by many as incurable, the acetabular disarticulation performed in this case with the removal of a slowly growing chondrosarcoma in its gross entirety may offer some hope although the same operation carried out at an earlier date would have proved a better chance of a cure.

The highly malignant primary chondrosarcoma of the lower jaw leaves little room to question that a radical anterior resection of this bone was the most desirable treatment. A bone sarcoma in this location which reached walnut size in 9 months, and trebled this size during 6 weeks following biopsy, does not offer a good prospect of cure by any method. The operation was one of curettage and radiation. The only hope for amelioration by X-ray or radium therapy lies in the extremely rapid growth of the tumor and its undifferentiated chondroblastic cells, which may show a fair degree of roentgen susceptibility.

## SUMMARY

1 Nine cases of chondromyxomatous tumors are individually presented and described from a clinical standpoint. Six of these were malignant sarcomas, two chondromas, and one may be regarded as a circumscribed chondrosarcoma occurring in a toe.

2 The close histological relationship of these tumors is reason for seeking a connection between their clinical course and (1) deviations from a unity of structure, and (2) factors apart from their histological composition.

3 From these features are derived factors of prognostic value.

a Limitation by a capsule of cortical bone, characteristic of the chondromyxomatous tumors of the small bones of the hand and foot, is usually accompanied by a slow, localized growth.

b A predominantly myxomatous tissue is less invasive and more slowly growing than that in which a greater differentiation of cartilage cells has occurred. Although the standpoint that myxomatous tissue is the least differentiated form of cartilage seems confirmed in these cases, the implied contradiction may be explained by an inhibitory effect of the myxomatous matrix on the cells which are contained in it, and by the view that bony differentiation depends partly on the matrix supplied for its formation by the destruction of bone by the less differentiated cells.

c The chondromyxosarcomas arising on the basis of a pre-existing osteochondroma or chondroma pursue a less rapid course after the assumption of a malignant character than those which are malignant from the outset. Although this corresponds to the statistics of Geschickter and Copeland, who find a strikingly greater percentage of 5 year cures in the secondary chondromyxosarcomas of their classification than in the primary form, the statistical evidence of the cases presented here is too limited, and much weight cannot be attached to this distinction as a factor in prognosis.

d An incomplete operation greatly accelerates the growth of a chondrosarcoma.

e The more proximal location of this type of tumor in a limb, or the existence of such a tumor in bone simultaneously undergoing normal developmental metaplasia or in the neighborhood of numerous structures arising from precartilaginous connective tissue, makes the prognosis less favorable.

4 The method of treatment used in this series of cases is discussed on the basis of the factors governing prognosis. Resistance to radiation, the beneficial effect of which lies chiefly in the

stimulation of reactive bone, makes this form of treatment useful only as a supplement to operation. Local, complete removal of an isolated, circumscribed tumor, which exhibits histologically a comparatively uniform structure, makes possible a more radical procedure should there be recurrence. For the outspokenly sarcomatous members of this group, a resection or amputation is advocated, as much as possible should be removed of the adjoining tissues which are composed of cells which exhibit stages in early cartilaginous development related to the tumor itself although of an orderly and normal architecture.

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## BIBLIOGRAPHY

- 1 ALESSANDRI, R. Recurrence of chondrosarcoma in transplant following bone resection. *Arch. di ortop.*, 1925, 41 No 1.
- 2 BAENSCH, W. Ueber die Grenzen des Knochentumornachweises. *Roentgenprax.*, 1931, vol 3.
- 3 BEHRING, I. A. R. Beitrag zur Kenntnis der Tumoren in den langen Rohrknochen, ihre Diagnose und Therapie. *Acta chirurg. Scand.*, 1930, vol 66.
- 4 BIRD, C. E. Sarcoma complicating Paget's disease of the bone. Report of nine cases, five with pathologic verification. *Arch. Surg.*, 1927, 14 No 6.
- 5 BLOODGOOD, J. C. Bone tumors. Myxoma. Second paper, with report of 3 new cases. *Ann. Surg.*, 1924, 80 No 6.
- 6 Idem. Treatment of bone sarcoma by toxins, radiation, amputation, or resection. *Am. J. Roentgenol.*, 1925, 14 No 3.
- 7 BORAK, J. Roentgentherapie bei Tumoren des Knochensystems. *J. Kurse artl. Fortbildg.*, 1928, vol 19.
- 8 CANIGIANI, T. Ein Fall multipler Knorpelgeschwulste des Skeletts mit oertlicher sarkomatöser Entartung. *Beitr. z. klin. Chir.*, 1933, 158 No 1.
- 9 CASTREN, H. Zur Kenntnis der metastasenbildenden Chondrome. *Acta Societatis Med. Fennicae* ("Duodecim"), 1931, 15 No 5.
- 10 CHRISTENSEN, F. C. Bone tumors. Analyses of 1000 cases with special reference to location, age, and sex. *Ann. Surg.*, 1925, 81 No 6.
- 11 COENEN, H. Die zentralen Knochenkrankungen. *Zentralbl. f. Chir.*, 1929, *Med. Klin.*, 1929.
- 12 GERSTEL and JANKER. Ueber die Entwicklung eines Spindelzellensarkoms auf dem Boden einer monostotischen Ostitis deformans Paget. *Deutsche Ztschr. f. Chir.*, 1933, vol 238.
- 13 GESCHICKTER and COPELAND. Tumors of bone. *Am. J. Cancer*, 1931.
- 14 GULEKE. Ueber die zentralen Chondrosarkome der Metaphysen. *Arch. f. klin. Chir.*, 174, 1933, vol 174.
- 15 HELLMER, H. Irrtümer der Diagnose bei Knochen-sarkomen und die Bedeutung der Probeexzision. *Arch. f. klin. Chir.*, 1932, 169 Dec.
- 16 Idem. Knochengeschwulste. *Zentralbl. f. Chir.*, 1933, 60 331.

7. HOFFMEIER, H. Erfahrungen über 3 Fälle von Knochensarkomen, welche mit Röntgenstrahlentherapie behandelt worden sind. *Strahlentherapie* 918, 919.
8. JUNGHEIMER, H. Ueber die Häufigkeit gutartiger Geschwülste in den Wirbelsäulen (Angiome Lipome Osteome). *Arch f klin Chir* 912, 69 Nov.
9. KATZ, E. Lehrbuch der speziellen pathologischen Anatomie. Vol. Berlin and Leipzig, 92.
10. KIRCHHOFF, R. Ein Fall von Chondrosarkom der Knochen. *Beitr klin Chir* 912, 91.
11. KIM. Ueber die neogenen Fenchondrome der Knochen. *Zentralbl f Chir* 913, p. 696.
12. KODONY, ANATOLE. Bone Sarcoma. Chicago: The Surgical Publishing Co. of Chicago, 927.
13. KONTZKY, G. E. Knochensarkome und ihre Begrenzung. *Arch f klin Chir* 913, 76 No.
14. LECOTY, LEE, BILL. Chondroma of the femur with repeated occurrences and ultimate death. *Arch Surg* 915, No.
15. LEMIRE, R. and POUSSARD, A. Considerations générales sur les ostéosarcomes, des relations existant entre les anomalies de l'ostéogénèse normale et la structure des sarcomes osseux. *Progrès Méd* 914, 915.
16. LINDER, E. Die Bedeutung des Bindegewebes für die Knochenregeneration. *Zentralbl f Chir* 913, 919, vol. 28.
17. LUCAS, G. Outcome des 21 brach ant nach Ellbogenverrenkung. *Polizei arz Chir* 919, 919.
18. MITSCHKE, ANTON. Ein sarcoma embryonale de une ombiliculaire musculaire traumatica para vertebral (change of parosteal osteoma to sarcoma). *Arch ital. Chir* 919, 5, 908-916.
19. PRINGSHEIM, D. B. Chondrosarcoma of bone. *Surg. Gynec. & Obst.* 919, 50, 6-33.
20. ROSS, L. Les anomalies des sarcomes osseux, etc. *Scapellato*, 919, 917-918.
21. SCHULZ, H. R., and ULLMANN, E. Zur Diagnose, Differentialdiagnose, Prognose und Therapie der primären Geschwülste und Zysten des Knochensystems. *Angewandte Strahlenforschung* 913, vol. 3.
22. Idem. Skapulagechwülste. *Röntgenport* 914, 4, 913-917.
23. SEIBT, J. Tumorartige Knochensarkome. *Arch f klin Chir* 913, 91 No. 4.
24. SIMON, W. A. Die Knochensarkome. *Ergebn d Chir Orthop* 913, vol. 6.
25. STEINHAUS, C. Lehrbuch der allgemeinen Pathologie und pathologischen Anatomie. Berlin, 913.
26. STEINHAUS, CARL. Personal interviews and communications, 913-914.
27. STEINHAUS, H. Kalkablagerungen in den Lungen unter dem Einfluß von Geschwulststrahlentherapie bei einem Sarkom des Schenkelbeins. *Zentralbl f Chir* 913, No. 18, Sept.
28. TROTTIER, L. Le traitement radiothérapique des ostéosarcomes. *Cancer* 919, 916.
29. WILHELM, R. Mehrfaches Vorkommen einer Neigung zu Knochenbrüchen und Sarkomentwicklung in einer Familie. *Zentralbl d Krebsforsch* 919, 919.
30. ZAWADZKI, W. Die Radiodiagnostik der Knochenneubildungen. *Polizei Med Chir* 919, No. 9.

# THE SURGICAL TREATMENT OF SEVERE FORMS OF LYMPHEDEMA (ELEPHANTIASIS) OF THE EXTREMITIES

## A STUDY OF END-RESULTS

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SEVERE forms of lymphedema, or elephantiasis, for many years have produced one of the most unsightly, and in many instances one of the most disabling, types of deformity. Particularly prevalent among women, whose cosmetic sense is more highly developed than that of men, it is the source of extreme mental suffering to those afflicted. From milder cases to cases of the most extreme enlargement of the affected part all grades of severity are encountered.

It is not our purpose in this paper to discuss the etiology of the condition. That phase of the question has been covered lately by Allen. Rather we propose to review methods of surgical treatment and to report the end-results from a study of cases in which treatment was given at the Mayo Clinic in the past 10 years. In all these cases a sufficiently long interval has elapsed since operation to be reasonably certain that final results have been obtained.

### REVIEW OF LITERATURE

In reviewing the literature on the surgical treatment of any disease one is invariably taken back to the era when this treatment was not based on the principle of correcting or relieving the underlying cause. So it is with the surgical treatment of elephantiasis. The earliest method of treatment probably was that of scarification, proposed by Lisfranc in the first half of the nineteenth century. Later, Carnochan (1851) ligated either the external iliac or femoral artery with the view of restricting the circulation and thus of decreasing edema. Improvement did not result and gangrene often followed. In the early part of the twentieth century, Dieffenbach, Mikulicz and others excised portions of affected skin and subcutaneous tissue, some temporary improvement followed, although it was questioned whether this was due to rest in bed or to the result of operation.

It was not long after reports of Dieffenbach's and Mikulicz' work appeared in the literature that surgical treatment of lymphedema assumed

an entirely different aspect. This, no doubt, had its origin in the discovery that the edema was due primarily to lymphostasis. Since the time that this knowledge was acquired, all surgical procedures have striven to provide a means of re-establishing the lymph flow or drainage. To Handley goes the credit for leading the way in this field, in 1908 he proposed a method of draining the obstructed regions into adjoining healthy tissues. He attempted to accomplish his purpose by inserting 4 long silk threads in subcutaneous tissue, the threads extending from the ankle to the deeper tissues of the abdominal wall. Later, Lexer modified the method by substituting strips of fascia for the silk threads, the results generally were unfavorable. However, more recently, Keysser, after trying several methods reported the best results from a combination of Lexer's and Handley's methods. Lefebvre (1926) has reported 26 cases in which patients were treated by this method with rather unsatisfactory results. Several years after Handley's work appeared, Walther further modified the method by burying a rubber tube between the deep fascia and the layer of muscle, the tube extended from the lower portion of the thigh to the lower portion of the abdomen. The lower end of the tube was left protruding through the deep fascia into the edematous tissue and the upper end was similarly placed in normal tissue. Following the operation, the extremity was elevated and bandaged. Ten cases were reported in which the results were satisfactory after a short time had elapsed. There were no later follow-up studies.

At the same time that Handley was trying to establish new lymph channels by the production of a reaction around a foreign material, others were approaching the situation from another angle. They were attempting to establish channels between deep and superficial tissues. Since deep fascia is not permeated by lymph channels, all procedures had to be directed either toward removing the fascia or making openings through it. Lanz was the first to devise a means of communication between superficial and deep tissues.

He made a longitudinal incision throughout the length of the thigh on the lateral surface. The incision extended downward through the fascia lata and intermuscular septum to the bone. The bone was then trephined and the marrow cavity opened in 3 places. Pedicled strips of fascia lata were then cut and inserted into the holes and attached to the openings in the marrow cavity. He hoped to establish drainage from the superficial tissues into the muscles and bones. In addition he made slits in the deep fascia. Lutz procedure was quite complicated, and the followers of his method dispensed with trephining the bone because it had no added advantage. Oppel was the first to make such modifications. He turned strips of fascia and edematous subcutaneous tissue in between the muscular layers and sutured them there. Furthermore, he extended the operation to the leg. Rosenow followed this same procedure, except that he turned triangular flaps in between muscular layers.

Kondoleon, about the same time and working on the same principle as Lutz, devised a simpler procedure which would accomplish the same end-result. He made a longitudinal incision the entire length of the extremity on both the lateral and medial aspects. The fascia was incised and its edges were sutured into the intermuscular septum. He later modified the operation by excising a strip of edematous tissue and fascia, about 5 centimeters wide from the entire length of the incision. The skin was allowed to drop down in contact with the muscles and the incision was closed without drainage. Six patients were treated by this method with good results. Still later however Kondoleon reported that the results were not so satisfactory as he had hoped, but that they were encouraging enough to justify operation in cases of marked lymphedema and elephantiasis. Kondoleon's technique was based on some experimental work in which he had shown that a broad communication must be established between the subcutaneous and muscular layer by removing the fascia which prevented such communication. If this was not done, one could not hope to clear the edema. The year following Kondoleon's description of his operative method, Matas made the most complete survey of the literature to be found, and he reported cases in which patients were treated by this method with satisfactory results. Later Burke reported 6 cases in which patients were treated by the Kondoleon method of these, end-results were given in cases. Six patients were definitely improved, the condition of 1 remained unchanged, and 4 were definitely worse.

Since Kondoleon first devised the operation, several modifications in the technique have been made but the general principle of the procedure has remained unchanged. Each successive modification has attempted to establish a broader communication between the deep and superficial tissues. Of all the various modifications, Sistrunk's has been followed by the most uniformly satisfactory results. He stressed pre-operative preparation, and this consisted essentially of rest in bed, with the extremity bandaged and elevated for 10 days to several weeks. After the patient had been properly prepared, the operation was carried out in 2 stages. One side of the extremity was operated throughout its entire length at the first stage and, 3 to 3 weeks later, the other side was operated. At the first operation an elliptical incision was made from the iliac crest to the ankle on the lateral surface and at the second operation, from the groin to the ankle on the medial surface, a sufficiently large piece of skin being removed to reduce the size of the extremity to almost normal. The margins of skin were then dissected back for a distance of 6 centimeters on each side, and edematous tissue incised downward through the deep fascia at this point. The skin edematous tissue and deep fascia down to the muscle were then removed in one piece. This allowed a broad communication between superficial tissues and underlying muscles. The skin was closed without drainage and a snug fitting bandage applied. Immediately following the operation, isotonic salt solution was given by rectum and subcutaneously. Morphine and ephedrine also were given as a further preventive of shock. Sistrunk's post-operative treatment consisted of the wearing of an elastic stocking or rubber bandage for an indefinite period of time. After about a year's time, an attempt could be made to discard the bandage, but if a swelling tended to recur the bandage was re-applied and worn until such time as it could be discarded without any resultant swelling of the extremity. If the swelling tended to recur even when the bandage was worn, the patient was placed in bed for a few days at intervals when the condition required it. In cases in which this regimen was followed, the results usually were favorable. Sistrunk reported 40 cases in which patients were treated by this method, 30 of these patients obtained good results and 10 were unimproved.

Several other modifications of the Kondoleon technique have been made, but all of these essentially were the same except that of Kimura. He performed the operation as prescribed by Kondoleon but, in addition, removed a long flap of

diseased skin and subcutaneous tissue close to its juncture with healthy tissue. He then turned down a pedicled flap of good skin and sutured it in the site where the diseased skin had been removed. Nine patients with involvement of the lower extremities were treated by this method with good results. More recently Professor De Gaetano suggested some modifications in the operation, however, these were similar to Sistrunk's except that De Gaetano did not remove as broad a strip of skin and fascia. Good results were reported. Battista has reported 2 cases in which treatment was by this method, and in both, results were good. Auchincloss made modifications in the Kondoleon technique which probably were a little more extensive than Sistrunk's. By his procedure all of the fascia surrounding the extremity could be removed by the 2 stage procedure. End-results were not given in this report. Later, Torgerson reported 5 cases in which patients were treated by this method. The results were good at the end of 6 months. Del Toro and Pons reported 12 cases of patients treated by this method, of these, 6 patients obtained fair results, 4 were not improved, and 2 were not followed.

Recently, Knutzen made a very extensive review of the foreign literature on the subject and discussed various types of operation. Sixteen cases in which operation had been performed were reported, of the patients, 2 obtained complete relief, 6 were greatly improved, 4 were slightly improved, and 3 received no benefit.

#### SELECTION OF CASES

The selection of cases for operative treatment is one of the most important factors leading to the success or failure of the operation. Severe cases of lymphedema of either extremity are all, of course, fit cases for operation, provided contraindications are not found on general examination. Recurrent attacks of cellulitis do not constitute a contra-indication to operation, although, of course, operation should be performed at times as far removed from the time of such attacks as possible. Patients with milder degrees of lymphedema in general are not good subjects for surgical treatment. In these cases the condition can be improved, but in most instances improvement is not as great as the patient expects and disappointment results. Many of these patients will need surgical attention later, however, unless a great deal of care is used in the wearing of the bandage. The patient should be warned that some form of supporting bandage or stocking must be worn after operation for an indefinite period.

#### PRE-OPERATIVE TREATMENT

Pre-operative treatment similar to that described by Sistrunk is prescribed. However, in our recent cases we have elevated the leg in a specially built sling (Fig 1). This sling is elevated so that the leg rests at an angle of 75 degrees from the horizontal plane of the patient's body when lying in bed. This elevation, together with bandaging and, if necessary, massage, is used without interruption, and the patient is not allowed out of bed. In this way edema may be greatly reduced in a few days, usually in not more than a week, and we are then able to proceed with the operation. The edema should be reduced before operation is attempted if a good result is to be obtained. The time required to clear edema will vary from 2 to 3 days in mild cases to a week or 10 days in very severe cases.

Under the routine of rest and elevation, any infection or ulceration which may be present will clear very rapidly. In any case, all superficial and deep infections should be cleared completely before operation.

In cases in which cellulitis has been a serious complication, and particularly in those cases in which rest does not reduce this infection promptly, much can be accomplished by immunization with antistreptococcic vaccines until the resting infection has subsided.

#### OPERATION

The operative technique we now use is essentially the same as Sistrunk's, with the exception that we follow the modifications that were proposed by Walters. These modifications are (1) the use of spinal anesthesia, (2) the use of a tourniquet, (3) the use of supportive treatments at the time of operation, and (4) allowing a longer interval to elapse between the 2 stages of operation, usually from 3 to 6 months. With the patient under spinal anesthesia, the entire extremity and lower portion of the trunk is prepared surgically. A tourniquet is applied as high up on the extremity as possible. The operation is carried out on the outer side of the extremity in the first stage. Two elliptical incisions are made throughout the entire length of the extremity and up to the iliac crest on the outer side. These incisions are about 8 centimeters apart at their widest separation and connect at each end. The flaps of skin are dissected back until nearly half of the circumference of the extremity is exposed. The edematous tissue and deep fascia are then incised down to the muscle layer. The subcutaneous tissue and deep fascia along with the skin are then removed in one piece leaving the broad region of muscle



Fig. Leg elevated in sling

bare. When the margins of skin are brought together the skin comes in direct contact with this large surface of muscle allowing a broad communication between these structures. The operation has been carried out so far in a dry field with the aid of the tourniquet but the tourniquet is now released momentarily to allow ligation of any bleeding points, and is then reapplied. The wound is then closed without any drainage. The tourniquet is again released for a moment and then reapplied. This procedure is repeated for several minutes, thus slowly restoring the circulation of the extremity. We believe that this slow return of the circulation in the extremity is a big factor in preventing postoperative shock. The extremity is then bandaged snugly and the patient is returned to bed. The extremity is not elevated, and the head of the bed is not lowered. Five hundred cubic centimeters of 6 per cent of acacia in physiological saline solution are given intravenously. Morphine sulphate or some other sedative is given for pain. Since the institution of this technique as herein described, the incidence of

TABLE I.—RELATION OF SEVERITY OF ELEPHANTIASIS TO IMPROVEMENT

Severity	Patients					Dead*	Dead to another cause	Total
	Improvement, grade							
Mild								
Moderate			20					20
Marked								11
Extreme								
Total			20					31
Per Cent		6	10			14		30

\*Dead from sepsis; shock; 3 from myocardial infarction 4 years after operation, 1 from embolus, 2 years after operation, and 1 from an unrelated condition (Dysphagia).

shock has been very low and no operative deaths have occurred.

#### POSTOPERATIVE TREATMENT

The dressing is changed at the end of 5 days and, if the wound is dry and healed, the stitches are removed. The patient is allowed to get out of bed at the end of 2 weeks if no complications have occurred. However before the extremity is placed in the dependent position, a snugly fitting elastic stocking or a para-rubber bandage is applied over its entire length. This support is worn for at least 1 year and until such a time thereafter as it may be discarded without return of the edema. If edema returns following operation even though the bandage is worn constantly, the patient is placed in bed for a few days until it subsides. When this outcome is achieved to closely by the patient, a good result will usually be obtained. However in a few of the severe cases, regions of thickened skin may have to be removed at some later date.

TABLE II.—RELATION OF WEARING OF BANDAGE TO IMPROVEMENT

	Patients							
	Dead*	Improvement graded			Lacks or no improvement Total		Improved Total	
					Number	Per cent	Number	Per cent
Wearing band long				17		56	72	
Wearing bandage questionable						73		
Not wearing bandage†				26		49		
Total			30	30	72	33	65	

\*All dead 4 years after operation.

†Most of three patients had only very mild elephantiasis of the foot on admission.

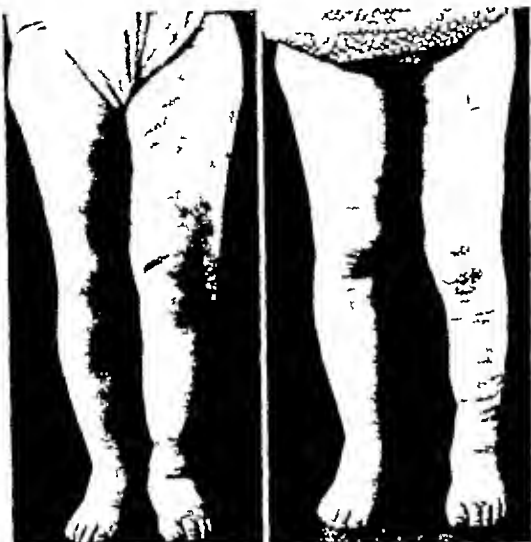


Fig 2 Left, Before last operation and, right, after last operation

#### CASES STUDIED

Sixty-four patients have been operated on at the Mayo Clinic by the modified Kondoleon method since Sistrunk's report of his technique in 1923. In this study we have followed these cases over a period of from 2 to 10 years. Of the 64 cases, end-results were learned in 55. In compiling these results, the information was secured by 2 methods, namely, by personal examination of the patient and by letters of inquiry after a sufficiently long period had elapsed following operation to determine the final result. It must be remembered, however, that data obtained by letter are not as reliable as those obtained by personal examination, in many cases, however, one has to depend on these data because of the inability of the patient to return for an examination. There is also a group of patients from whom one cannot get information by letter. Nine of our patients were in this group.

The improvement among patients whose cases were followed was graded on a basis of 0 to 4, the latter signifying almost complete relief (Table I, Figs 2, 3, and 4). According to this grading, the condition of 12.5 per cent of the patients was unimproved, that of 14 per cent was improved, Grade 1, that of 7.8 per cent was improved, Grade 2, that of 31.3 per cent was improved, Grade 3, and that of 10.9 per cent was improved, Grade 4. A mortality rate, both immediate and remote, of 9.3 per cent was noted. The 3 postoperative deaths made an operative mortality of 4.7 per cent. Further analysis of the cases revealed



Fig 3 Left, Pre-operative and, right, postoperative appearance

that there was very slight relationship between the severity of the disease and the degree of improvement.

A satisfactory degree of improvement was noted in 42.2 per cent of the cases, whereas in 21.8 per cent there was some improvement, although not enough to be called very satisfactory. These results were influenced by the wearing of an elastic supporting stocking of some sort. We have



Fig 4 Left, Before last operation and, right, after last operation



TABLE III—RELATIVE INCIDENCE OF INFECTION BEFORE AND AFTER OPERATION

Infection	Patient						
	Before operation	After operation					
		Dead	Reinfect	More serious	Ulc. supp.	Im. proved	Chained
Phleboma		1*		2			
Celulitis							
Erysipelas		1					
Embolus							
Total	26						

\*Dead from embolism—year after operation

†Dead 4 years after operation

‡A small ulcer developed in areas in which the patient had not suffered from infection before the operation.

already stated that some form of supporting bandage must be worn after operation. Thus, it is seen (Table II) that real improvement was found in 72.5 per cent of those cases in which the patients were known to be wearing a bandage after operation, whereas in only 40 per cent of those cases in which a bandage was not worn was the condition improved.

The relative incidence of infection before and after operation showed marked improvement. Of 26 cases in which the patients were suffering from recurrent attacks of infection of some sort, in only 6 was the infection worse or unchanged, whereas in 9 it was much improved, and in 11 it had completely disappeared (Table III).

## COMMENT

Practically every one of the succeeding modifications of the original Kondoleon operation has been accompanied by some improvement in the results obtained. The principle of the operation, however, has remained unchanged, namely, of establishing a communication between the deep or muscle layer and the subcutaneous layer. The conception that this procedure resulted in a communication between the superficial and deep lymphatic systems has been discarded, and it is now thought that the superficial lymph vessels drain directly into the vascular network of the muscles. Each of the succeeding modifications has striven to increase the communication between these regions.

Sistrunk made the greatest advance in accomplishing this end when he removed a much wider strip of edematous tissue and fascia as well as a strip of skin. This modification was followed by

much improvement in the results. All other changes have added very little to the extensive news of the operation. Additional modifications have been made in Sistrunk's technique which have simplified the operation from the standpoint of severity and led to more satisfactory results. Adequate preparation is very important because, if edema is not controlled prior to operation, the procedure is much more difficult, the fascia usually is not so extensively resected, and the results are not as good. For this reason we stress rest in bed until edema has completely subsided.

The use of the tourniquet has proved very valuable in our cases. Bertwistle and Gregg, on the other hand, found the tourniquet to be of no value. Its failure in their cases was probably due to insufficient pre-operative preparation, that is, the edema of the extremity had not been controlled. Torgerson did find the tourniquet very valuable. Since we began to use the tourniquet the incidence of shock has been reduced to a very small percentage and no operative deaths have occurred. It must be remembered that the slow release of this tourniquet over a period of several minutes is also a big factor in the prevention of operative shock.

In the postoperative care of these patients, many failures to obtain a good result are due to the patient's neglect in wearing a support. Often the problem arises of sufficiently impressing these patients with the necessity for wearing the bandage. If one is patient enough, however, this point can be impressed on almost all of them; it must be done if a satisfactory result is to be expected. If the bandage is worn continuously when patients are on their feet, the results are usually favorable. Occasionally the swelling will tend to return for some time after operation; in such cases a few days' rest in bed will control it.

## BIBLIOGRAPHY

- ALLRED, E. V. Lymphedema of the extremities. *Proc. Staff Meet. Mayo Clin.* 1934, 0: 3-5.
- ALONSO, R. R. A new operation for elephantiasis. *Ann. Porto Rico J. Pub. Health Trop. Med.* 1929, 4: 149-50.
- BARTON, A. Surgical cure of elephantiasis. *Urol. & Cutan. Rev.* 1930, 34: 43-49.
- BERTWISTLE, A. P. and GREGG, A. L. Elephantiasis. *Brit. J. Surg.* 1928, 6: 807-12.
- BONICK, G. R. Results in Porto Rico of Kondoleon operations for elephantiasis of extremities. *Surg. Gynec. & Obst.* 1928, 47: 843-847.
- CARDONA. Quoted by Miles.
- DIERCKMANN and MINKOWICZ. Quoted by Keyser.
- DE OLIVEIRA, L. Sozinha cura cirurgica della elefantiasi degli arti inferiori. *Riforma med.* 1928, 44: 765-765A.
- HANDLEY, W. S. Lymphangioplasty. *Lancet, Lond.* 1903, 753-754.

- 10 KEYSER Zur operativen Behandlung der Elephantiasis Deutsche Ztschr f Chir, 1927, 203-204 356-375
- 11 KIMURA, H On the treatment of elephantiasis Japan Med World, 1925, 5 201-211
- 12 KNUTZEN, HEINRICH VII. Die chirurgische Behandlung der Elephantiasis Ergebn d. Chir u Orth, 1929, 22 431-461
- 13 Idem Die Chirurgie der Elephantiasis klinische, histologische und experimentelle Untersuchungen Arch f klin Chir, 1930, 158 543-583
- 14 KONDOLEON, E Die Lymphableitung, als Heilmittel bei chronischen Oedemen nach Quetschung Muenchen med Wchnschr, 1912, 59 525-526
- 15 Idem Die chirurgische Behandlung der Elephantiasischen Oedeme durch eine neue Methode der Lymphableitung Muenchen med Wchnschr, 1912, 59 2726-2729
- 16 Idem. Die operative Behandlung der Elephantiasischen Oedeme Zentralbl f Chir, 1912, 39 1022-1024
- 17 Idem. Ultimate end results of Kondoleon operation for elephantiasis edema Arch franco-belges de chir, 1924, 27 104-110
- 18 LANZ, O Eroeffnung neuer Abfuhrwege bei Stauung im Bauch und unteren Extremitaeten Zentralbl f Chir, 1911, 38 153-155
- 19 LEFEBVRE, C Le traitement chirurgical de l'éléphantiasis des membres J de Chir, 1923, 21 434-458
- 20 LEXER, E Erworbenes Elephantiasis Muenchen med Wchnschr, 1919, 66 1274.
- 21 LISFRANC. Quoted by Keysser
- 22 MATAS, RUDOLPH The surgical treatment of elephantiasis and elephantoid states dependent upon chronic obstruction of the lymphatic and venous channels Am J Trop Dis. & Prev Med 1913, 1 60-85
- 23 OPEL, V A Quoted by Rosanow
- 24 ROSANOW, W N Lymphangioplastik bei Elephantiasis Arch f klin Chir, 1912, 99 645-655
- 25 SISTRUNK, W E Further experiences with the Kondoleon operation for elephantiasis J Am M Ass, 1918, 71 800-806
- 26 Idem The Kondoleon operation for elephantiasis A report of end results South M J, 1921, 14 619-625
- 27 Idem Elephantiasis. Surg Clin N America, 1921, 1 1523-1529
- 28 Idem The Kondoleon operation for elephantiasis A report of end results Med Rec, 1921, 99 75
- 29 Idem The results obtained in elephantiasis through the Kondoleon operation Minnesota Med, 1923, 6 173-177
- 30 Idem. Certain modifications of the Kondoleon operation for elephantiasis Ann Surg, 1927, 85 190-193
- 31 TORGERSON, W R. Preliminary report on the Auchincloss operation for elephantiasis Porto Rico J Pub Health & Trop Med, 1931, 6 411-418
- 32 DEL TORO, JORGE, PONS, J A, and MOLINA, R. R Case report on twelve Auchincloss or modified Auchincloss operations for filariasis Porto Rico J Pub Health & Trop Med, 1931, 7 3-10
- 33 WALTERS, WALTERMAN Personal communication to authors.
- 34 WALTHER, C Buried tube drainage of elephantiasis Bull de l'Acad de méd, 1919 86 262

## THE CORRECTION OF HIP FLEXION DEFORMITY IN ANTERIOR POLIOMYELITIS

### A RESULT STUDY

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THIS study is based on hip flexion deformities in 130 children treated at the Shriners Hospital for Crippled Children at Springfield, Massachusetts from its opening in February, 1925 to November 1, 1933.

We agree with previous authors that this condition is one of the most disabling distortions complicating infantile paralysis (1). Even a mild degree of deformity contributes markedly to the limp and functional disability while a deformity of more than 30 degrees produces a distressing exaggeration of the lumbar lordosis. More extreme deformity may be sufficiently crippling to prevent walking, and to limit the unfortunate individual to a wheel chair existence.

In common with other paralytic deformities, hip flexion, which is commonly a combination of flexion and abduction, is produced by imbalance of antagonistic muscles with adaptive shortening of the relatively stronger muscles. The deformity is further aided and abetted by habitual flexion in sitting and in recumbency. The characteristic inherent property of muscle tissue to contract when insufficiently opposed produces a structural shortening of the hip flexors namely the tensor fasciae latae, sartorius, rectus femoris, anterior portion of the gluteus medius and minimus, and the iliopsoas. These are enumerated in what appears to us to be their relative importance in producing the deformity. Occasionally there may be changes in the capsule of the hip joint preventing correction, but we have not met any such cases.

We have included in this series, 9 children with paralysis due to lesions of the spinal cord, since the nature of the deformity is the same as in poliomyelitis. Six of these were due to spina bifida, 3 being complicated by large sacral meningoceles. The others were due to birth trauma. Eight of these cases were bilateral making a total of 17 deformities. The meningoceles were also repaired.

#### INCIDENCE

The incidence of hip flexion deformity as occurring at this clinic is shown by the fact that during this same period 61 cases of infantile paralysis were admitted. The deformity was found in approximately 9 per cent or 1 of every 5 cases.

The deformity was seen more often in boys than in girls with a sex ratio of 32 boys to 48 girls, or 63 per cent males to 37 per cent females. There were 38 bilateral cases equally divided, with 19 males and 19 females. Consequently the total 168 deformities were 101 boys, or 60 per cent, and 67 girls, or 40 per cent.

In 64 cases, or approximately 38 per cent, the correction of hip flexion was the only surgical procedure undertaken at the time of operation. In the 104 remaining corrections, or 62 per cent, some other concomitant surgical procedure was carried out.

The deformity may occur at any age throughout childhood, being seen in these cases as early as 2 months, and in 10 instances under 3 years. From the age of 3 to 15 the incidence was fairly constant with about 10 cases in each year period, with slightly greater incidence between the ages of 5 and 10 years.

The deformity may also occur very early after the onset of paralysis unless particular precaution is taken to recognize the danger and prevent it by proper splinting and physiotherapy. In this series one patient developed a deformity of 30 degrees in only 4 months. In about one-half of the cases paralysis had been present from 3 to 5 years with approximately 30 per cent less than 3 years and 30 per cent more than 5. From 6 to 14 the distribution was practically the same for each year. Within limits, the deformity tends to be proportional to the duration of paralysis and is progressive to a certain extent. The most marked deformities, however, in this group were from 8 to 10 years' duration.

The amount of deformity when recorded in degrees varied from 10 to 90 degrees and averaged about 40 degrees. An extreme deformity that is 60 degrees or more, was present in 20, or 19 per cent of the numerically recorded cases. This is somewhat less than Speed reported in his series in which he found a deformity of 60 degrees or more in 24, or 34 per cent, of 70 cases under 15 years of age. A moderate deformity (30 to 60 degrees) was present in 69 cases, or 61 per cent while 24 cases, or 20 per cent, showed a mild deformity of less than 30 degrees.

## CORRECTIVE PROCEDURES

Five methods of correction of the deformity were used in these cases, namely (1) stretching alone, (2) subcutaneous tenotomy of the structures at the anterior iliac spine, (3) subcutaneous tenotomy of the iliotibial band above the knee, (4) open division of the iliotibial band, and (5) fasciotomy of the hip. These methods were combined in varying ways making a total of eight groups of procedures. In addition to the five listed, (6) a subcutaneous division of the iliotibial band was combined with a fasciotomy of the hip and (7) open division of this structure was combined with subcutaneous fasciotomy at the hip or (8) with open fasciotomy. Each of these groups will be considered individually, with the results and analysis of failures in those cases which have been observed for a minimum of 1 year.

## STANDARD OF ESTIMATING RESULT

The result in each case has been classified as either good or poor. A good result was considered to be a case in which complete extension in both abduction and adduction has been maintained for at least 1 year. The selection of this time limit is arbitrary, since only 33 per cent of the recurrences have occurred during the first year, 33 per cent occurring during the second year, while one-third have appeared as late as 4 to 6½ years after correction. However, the exclusion of the 18 cases followed less than 1 year eliminates no failures, while 10 of the total 30 poor results are among the 39 cases followed between 1 and 2 years. Consequently, the arbitrary minimum of 1 year was imposed. With selection of corrective procedure there have been no difficulties encountered in obtaining complete over correction in all cases. There has been no operative mortality and no complications. We believe this to be due in part at least to gradual postoperative stretching rather than immediate fixation. The chief problem is in maintaining rather than obtaining correction.

## STRETCHING

Simple stretching was used alone in 2 cases. Both were girls with mild deformity, slight in one and 15 degrees in the other. The first (W G 530) was 10 years old and had had paralysis for 1 year. She was hyperextended for 4 weeks. Four years later, however, she returned with a deformity of 35 to 40 degrees, requiring operation. The other patient (N B 619) has maintained her correction for 2 years. She was 6 years old and had had paralysis for 4 years when corrected. The fact that this method of correction has been attempted

in only 2 instances indicates our agreement with the general opinion that stretching methods are ineffective. Even with favorable selection, the results are only 50 per cent satisfactory.

Postoperative stretching, however, is a very important part in the care of these cases, and this has been carried out for a varying period in all cases. A long leg plaster is applied to the affected leg and, as soon as the postoperative reaction is over, the hip is gradually hyperextended by dropping the leg through an elevated Bradford frame from which the lower canvas has been removed. The pelvis is controlled by a plaster jacket or by flexion of the good hip in unilateral cases.

## TENOTOMY AT THE ILIAC SPINE

Subcutaneous tenotomy of the structures attached to the anterior superior iliac spine was done alone in only 3 cases, indicating our agreement with Steindler and others that such procedures are generally insufficient. In one case (V B 1373), a girl of 10 years, with paralysis for 4 years, showed only a mild deformity which was originally corrected by open division of the iliotibial band and subcutaneous tenotomy at the hip. After 1 month of postoperative stretching, there was still a deforming band present which was divided. However, the procedure was still unsatisfactory as the deformity recurred after 1 year. The other two hips were associated with dislocation in a 4 year old boy (R H 2248) with spina bifida. Tenotomy was done preliminary to closed reduction, and the child has been followed for less than a year since the correction.

## TENOTOMY OF THE ILIOTIBIAL BAND

Subcutaneous division of the iliotibial band was done twice alone, and three times combined with an open fasciotomy of the hip. The first two were in young boys (R S 498 and W MacD 979), aged 4 and 2, with paralysis of 3 and 1½ years' duration. Correction has been maintained for 6 and 4 years since operation. The other cases (K. W 1598 and V DeB 2015) were 7 and 10, with paralysis of 4 and 5 years. The deformities were 40 degrees. Correction has been maintained 2 and 1 years. In spite of these results, we feel that the procedure is rarely to be recommended, as it is difficult if not impossible to divide the deep intermuscular septum completely without adequate exposure.

## OPEN DIVISION OF THE ILIOTIBIAL BAND

Open division of the iliotibial band was done alone 40 times in 34 children. The procedure used was that described by Yount in 1923. The lower

part of the iliotibial band is exposed immediately above the knee joint and divided transversely. The extension deep in the intermuscular septum is completely divided and the periosteal attachment to the femur reflected upward. The wound is then closed with subcutaneous and skin suture. During the procedure the leg is held in adduction and maximum extension which makes the deforming band stand out prominently. The operation is simple, short, and can be done under novocain infiltration if desired.

The age of the patients having this procedure alone varied from 15 months to 15 years, with two major groups of about one-third each from 6 to 8, and 13 to 15 inclusive. The duration of paralysis varied from 4 months to 14 years with most of the cases from 1 to 5 years. In the 23 measured deformities, the angle of deformity varied from 10 to 70 degrees, with 30 per cent of the cases under 30 degrees, 57 per cent from 30 to 60, and 13 per cent 60 or over.

There are available for follow-up study 31 cases with 35 operations, which have been observed over a period of from 1 to 8 years. Nine have been examined one year after operation, 8, two years after, 6, three, 4, four, 2, five, 1, six, 4, seven, and 1, eight.

The following 5 cases (14 per cent) have shown a recurrence of deformity.

**CASE 1.** Girl, of 8 years (D. P. 095) had had paralysis for 3 years. The deformity was bilateral and amounted to 30 degrees on the right and 40 degrees on the left. The extensors were absent, the flexors good. The right leg had an open division of the iliotibial band alone, while the left in addition had a subcutaneous tenotomy of the structure attached to the anterior superior iliac spine. Hyperextension was difficult to obtain and she was stretched for 8 weeks after operation. The paralysis was very extensive, but the child, as made ambulatory with bilateral caliper braces and crutches. She walked very little, however, and 5 months after operation beginning recurrence was noted. Two years after operation the deformity amounted to 30 degrees on the right and 45 degrees on the left. She was then readmitted and the deformities were again corrected by hip fasciotomy on the left and combined fasciotomy and division of the iliotibial band on the right. She was again hyperextended for 8 weeks, but 6 months later the deformity had again recurred bilaterally. The important factor in the failure in this case, as the lack of co-operation of the patient and her parents, who seemed satisfied to permit heel chair existence in spite of their protests to the contrary.

**CASE 2.** An infant corrected at 5 months of age (I. W. 4) had had paralysis for 3 months and presented 40 degrees of deformity. The extensors were absent, the flexors fair. She was lost from observation for considerable period, but at the age of 6, 5 years after the correction, she was found to have 30 degrees of hip flexion deformity.

**CASE 3.** A 3 year old boy (A. P. 33) had had paralysis since the age of 3 months. At time of operation he presented 30 degrees of deformity. The extensors and flexors were both rated as fair. He maintained his correc-

tion for considerable period but at the age of 6, 3 1/2 years after operation, he was found to have deformity of between 30 and 30 degrees.

**CASE 4.** Girl of 3 1/2 years (E. B. 718) had had no acute attack at the age of 6 months. She had deformity of 33 degrees at the time of operation. The extensors were rated as poor while the flexors were fair plus. She maintained her correction for 4 years when recurrence of 5 degrees was noted on examination. This was corrected by combined fasciotomy and division of the iliotibial band and correction has been maintained for 1 year.

**CASE 5.** A 5 year old boy (J. P. 708) with paralysis for 3 years had bilateral deformity. The extensors were totally paralyzed, the flexors were poor. He has been observed for 7 years and while the right is still completely corrected, the left hip shows very slight recurrence.

Two other cases in this group are of particular interest as they represent failures of previous correction. The first is a girl (W. G. 530) of 14 years with paralysis of 5 years' duration, and bilateral deformity. Four years previously her deformity had been corrected in this clinic by stretching. The other case, also a girl (E. F. 424), was 15 years old with paralysis of 1 year's standing and slight bilateral deformity. The extensors were poor and the flexors absent. Eight years previously she had bilateral correction apparently by Soutter fasciotomies at the Boston Children's Hospital. She has maintained her correction for 7 years since her second operation.

#### HIP FASCIOTOMY

Fasciotomy of the hip was done 45 times on 37 children. The procedure employed is a modification of Soutter's method which he presented in 1914 (2). The anterior superior iliac spine is exposed through an oblique incision 2 to 3 inches long extending from immediately below the spine obliquely toward the trochanter. The spine is denuded and the attachments reflected down as far as the anterior inferior spine. The contracted fascia over the tensor fascia femoris is divided transversely and the wound closed with subcutaneous and skin sutures.

The age of these patients is somewhat greater than where the iliotibial band alone was divided.

Living from 1 to 5 years with about one half 10 years old or over. The duration is slightly longer, varying from 1 to 14 years with about one half 6 years or more. and the deformity is a little more severe, varying from 20 to 80 degrees with half the cases showing 45 degrees or more deformity. Thirty 8 cases with 4 operations are available for follow up having been observed from 1 to 7 years. The period of observation was 1 case for year 1, for 3 years, 5 for 5, 8 for 6 and 4 for 7 years. Nine cases, or 3 per cent, showed recurrence of deformity. This may be compared

with Steindler's (2) report of his results in 75 cases of hip flexion corrected by the Soutter method observed over 1 year. Using the same standard as that on which we insist, namely, complete extension in abduction and adduction, he found good results in 66 cases, or 88 per cent, and poor results in 9 cases, or 12 per cent. Speed, in a series of 120 operations by Campbell's technique, obtained 83 per cent good results.

The 9 failures include 7 single cases and 1 bilateral. These were 3 girls and 6 boys.

CASE 1. D. P. 1056 has been cited under open division of the iliotibial band.

CASE 2. A boy (I. C. 419) aged 9 years at the time of operation, had had paralysis for 7 years and presented a deformity of 30 degrees. Muscle test showed extensors poor, flexors normal. Four years after operation a slight contracture in abduction was noted. The slight amount of shortening which was present, however, compensated the abduction, so that it was not functionally disturbing. During 3 more years of observation the deformity has not increased.

CASE 3. A boy (S. T. 244) aged 7 years had a paralysis of 5½ years' duration and a deformity of 20 degrees. Muscle test showed extensors fair, flexors normal. One year after operation a recurrence of 15 degrees was observed, which increased to 20 degrees and was corrected by a second fasciotomy 4 years later. Correction has been maintained for 1 year following the second operation. This child also presented a recurring knee flexion deformity more severe both functionally and anatomically than the hip deformity, which was also corrected at both admissions.

CASE 4. A boy (R. D. 974) aged 11 years with paralysis due to spinal cord injury, at birth with hip flexion deformity of 60 degrees on the right and 65 degrees on the left. One year and 9 months after operative correction a deformity of 30 degrees was noted at the right hip, the left still being fully correctable.

CASES 5 and 6. An 11 year old girl (V. B. 1373) had a paralysis of 5 years' duration, with bilateral deformity. One year previous to this operation she was admitted for a similar deformity of 40 degrees at each hip. Correction was attempted on both sides by open division of the iliotibial band and subcutaneous tenotomy at the anterior superior iliac spine. Postoperative stretching was continued for 4 weeks, when a tight band which prevented hyperextension on the left was divided by a subcutaneous fasciotomy at the hip. Six months later a recurrence of deformity at the right hip was first observed, and in 2 months more this was noted on the left. One year after the first correction the deformity amounted to 40 degrees on the right and 20 degrees on the left. Open fasciotomies were done and the deformities again corrected. Three months later 30 degrees of flexion deformity was again found to be present and this has persisted for 2 years.

CASE 7. A boy (E. C. 668) of 7 years, with paralysis for 3 years, was corrected by a hip fasciotomy. Hyperextension was present for 4 months but 1 year later 30 degrees of flexion deformity had recurred. Eighteen months after the first operative correction, the procedure was repeated. This correction has been maintained for 1 year.

CASE 8. A boy (R. B. 2080) of 6 years with acute onset of paralysis 5 years before, presented a deformity of 50 degrees. Extensors rated fair minus and flexors fair plus. Correction was obtained and the hip stretched in hyper

extension for 5 weeks. One year later a recurrent deformity of 20 degrees was noted.

CASE 9. A boy (D. L. 1351) of 3 years had very extensive paralysis at age of 6 months. During the subacute stage he was hospitalized for a period of 10 months with protection and muscle training. Considerable improvement was obtained in arms, but very little in trunk and legs. Four months after discharge he was found to have developed a flexion deformity of the hip, and 7 months later he was readmitted and a fasciotomy performed. Correction was maintained for 7 months but when examined 16 months after operation a recurrence of deformity was noted.

Two other cases, although not representing failures, are of interest.

A 5 year old boy (H. W. 690) had an acute attack when 3 months old. At operation he presented a hip flexion deformity of 45 degrees which was corrected. One year later the deformity showed a slight tendency to recur and home stretching was instituted. No deformity developed and he has maintained full correction for 7 years.

One girl (M. L. 438) of 15 years with extreme paralysis of 8 years' duration showed a bilateral deformity of 90 and 70 degrees. She had been operated on for a similar deformity at the Boston Children's Hospital 8 years previously. She had a combined procedure on the right and a simple fasciotomy on the left and was stretched for 10 weeks. There is full correction 2 years after operation, but she stands with extreme lumbar lordosis and complains of intermittent low lumbar backache.

#### DIVISION OF ILIOTIBIAL BAND AND TENOTOMY AT THE HIP

Open division of the iliotibial band as previously described was combined with subcutaneous tenotomy of the structures attached to the anterior superior iliac spine 28 times in 22 children. These were largely cases in which the first procedure failed to give satisfactory immediate correction, but where the remaining deformity was thought to be insufficient to demand the complete division of an open fasciotomy. In these cases, the age varied from 2 to 14 years, with half under 6 years and three-quarters under 9. The duration of paralysis from 1 to 6 years, with half 4 or more, and the amount of deformity in 17 recorded cases varied from 20 to 60 degrees with half 45 degrees or more. Twenty four operations in 19 cases are available for follow up, having been observed for 1 year in 8 cases, 2 years in 10 cases, and 3 years after operation in 6 cases. Nine cases (37.5 per cent) in 7 children showed recurrence of deformity.

CASE 1. D. P. 1056 has been cited under division of the iliotibial band.

CASES 2 and 3. V. B. 1373 see under hip fasciotomy.

CASE 4. A girl of 19 months (H. P. 2237) with paralysis of 16 months, had this procedure followed by 8 weeks of stretching. This, however, was found to be inadequate to secure complete correction and a fasciotomy at the hip was done. Correction has been maintained for 1 year.

CASE 2. A 2 year old boy (C. O. 367) with no definite history of the acute attack was corrected by this method and maintained correction for 14 years when slight recurrence was noted. Muscle test showed poor extensors and fair flexors. During the next year the deformity did not increase.

CASES 6 and 7. Another 2 year old boy (A. L. 346) with paralysis for 2 years, presented 5 degrees deformity in both hips. These were corrected, and correction maintained for 1 year and 3 months when recurrence was noted of 5 to 10 degrees on the right and 20 degrees on the left.

CASE 8. A 9 year old boy (N. H. 1466) with paralysis for 3 years presented 45 degree deformity. Muscle test showed absent extensors and good flexors. He was stretched for 2 weeks following correction. One year later deformity of 10 degrees had returned. Two years after operation a second correction was done by hip fasciotomy and this has been maintained for 7 years.

CASE 9. A boy (A. S. 318) aged 1 year, with paralysis of 4 1/2 years, had been admitted with flexion deformity of the left hip. 14 years previously which had been corrected by open division of the iliotibial band combined with subcutaneous fasciotomy of the anterior superior spine. He was stretched for 4 weeks after operation. Nine months later recurrence of abduction deformity was noted, and 3 months after the first operation, second correction was done by hip fasciotomy. This correction has been maintained for 7 years. Muscle test before the second operation showed good extensors and trace in flexors, but no adductors.

#### DIVISION OF ILIOTIBIAL BAND AND HIP FASCIOTOMY

Open division of the iliotibial band and open fasciotomy of the hip were combined 45 times in 37 children. These represent on an average older children, with paralysis of longer duration, and more severe deformities. The age varies from 2 to 15 with three-quarters 8 or over. Approximately one-half had paralysis more than 5 years.

The amount of deformity was mild or less than 30 degrees in 6 cases, moderate or 30 to 50 degrees in 21 cases, and severe or 60 to 90 degrees in 13 cases. The period of postoperative stretching in 33 hips varied from 3 to 14 weeks, being usually 4 weeks.

Forty-two operations on 35 patients have been followed for more than 1 year. The period of observation has been 8 years in 3, 7 years in 4, 6 years in 4, 5 in 4 in 6, 3 in 10 in 6 and 2 in 8 cases. There have been 5 recurrences in this group, or an incidence of 12 per cent.

These failures were as follows:

CASE. A girl of 2 years (C. S. 1010) with paralysis for 14 years and 3 degrees deformity. The extensors were poor and the flexors good. She was stretched for 4 weeks after operation. A recurrence of 3 degrees was noted between and 15 years after operation. This was corrected by intermittent stretching at home and remanaged corrected about 5 years after her original operation when 10 degree deformity in full abduction was again noted.

CASE. A boy of 8 years (D. I. 348) who had had paralysis for 5 years, had 40 degree deformity which was

corrected and stretched for 3 weeks. There was no power in either flexors or extensors. One year after operation deformity of 10 to 15 degrees had reappeared and this has remained constant for 7 years.

CASES 3 and 4. A boy of 8 years (E. A. 1013) with acute onset of his paralysis at the age of 1 year, presented deformity of 80 degrees on the right and 90 degrees on the left. The only demonstrable hip musculature was poor flexors on the right. Correction was maintained for 7 years on the right and 4 years on the left, before slight recurrence appeared. He had been followed for 4 years and the deformity in the right has not increased.

CASE 5. The details of this case (D. P. 1070) have been given under open division of the iliotibial band.

Another interesting case in this group is that of a boy of 12 years (J. D. 404) with a paralysis of 10 years standing and a deformity of 60 to 75 degrees who had a similar deformity corrected at the Boston Children's Hospital 7 years previously. He has maintained his second correction for 6 years.

Of particular interest in this series is a group of eight deformities in boys in whom division of the iliotibial band and stretching for from 3 weeks to 4 months (average 6 weeks) was insufficient to obtain hyperextension. These boys then had the fasciotomy done at the hip and have maintained their corrections 8, 7, 3, 2, 4, 1 and 2 years, respectively. At operation they were 9, 9, 15, 12, 3, and 8 with paralysis of 3, 5, 0, 12, 7 and 5 years standing. The deformity was 60, 45, un stated, 30, 80-90 and 30-35.

#### ANALYSIS OF FAILURES

Correction was obtained in 168 deformities. Eighteen of these all of which still show complete correction, are excluded, because they have been observed less than 2 year since operation. Of the 150 remaining cases, which have been followed from 1 to 8 years, 30 (20 per cent) have shown some recurrence of deformity. This recurrence has appeared during the first year in about one-third of the cases, during the second year in another third, and the remainder have been late, 4 at 4 years, 1 at 5 and 1 at 8 1/2 years after correction. The recurrences have been equally divided between the boys and girls and as the deformity was found more frequently in boys, the index of recurrence is slightly greater in the girls.

In regard to the type of correction there would seem to be evidence that open operations offer better probability of success than subcutaneous divisions.

It is of particular interest that the recurrence did not seem to be influenced by the severity of the deformity but that the contrary seems to be true. In 2 extreme deformities (60 to 90 degrees)

there were only 3 failures, or an incidence of 13 per cent. In 69 moderate deformities (30 to 59 degrees), there were 12 failures or 18 per cent, while in 23 mild deformities (less than 30 degrees) there were 7 failures, or 30 per cent.

We had also a preconceived idea that the older patients with longer duration of paralysis would probably show greater recurrence. This, however, was not found to be true. In 20 cases correction was done at ages younger than 4 years, and of these 9 showed recurrences, or 45 per cent. Forty-eight cases aged 10 or over showed 10 poor results, or 20 per cent.

In the whole series, 20 per cent were under 3 years, while of the recurrences 30 per cent were of this age. Thirty per cent of the entire group were above 5 years, while 20 per cent of the recurrences were above this age. There is no significant difference of the age of onset of the paralysis in the entire group and in the recurrences.

#### SUMMARY

1 Hip flexion deformity, which is actually a combination of flexion and abduction, is a disabling and common complication of infantile paralysis, occurring in 19 per cent of 622 cases seen at this clinic.

2 It may occur alone or in combination with other deformities. Some other deformity corrected at the same time was present in 62 per cent.

3 In this series the ratio of male to female is 60:40.

4 The deformity may occur at any age during childhood, and may appear early in the disease although most commonly seen 3 to 5 years after onset. The deformity may increase up to 90 degrees of flexion.

5 Five methods of correction have been employed, combined to form eight groups, namely, stretching, subcutaneous tenotomy at the hip, subcutaneous tenotomy of the iliotibial band, this procedure combined with fasciotomy at the hip, open division of the iliotibial band, this combined with subcutaneous tenotomy at the hip, the same combined with fasciotomy at the hip, and fasciotomy at the hip alone. Over 95 per cent of the cases encountered are included in the last four groups.

6 Stretching is considered a factor of great importance in the postoperative care of the patient.

7 The standard accepted for a good result has been complete extension in both adduction and abduction for at least 1 year following operation.

8 The results obtained have been as follows: Stretching, 2 cases. Available for result study, 2. Good results, 1, 50 per cent. Poor results, 1, 50 per cent.

Tenotomy at hip, 3 cases. Available for result study, 1. Good results, none, 0 per cent. Poor results, 1, 100 per cent.

Tenotomy of iliotibial band, 2 cases. Available for result study, 2. Good results, 2, 100 per cent. Poor results, none, 0 per cent.

Tenotomy of iliotibial band combined with fasciotomy at the hip, 3 cases. Available for result study, 3. Good results, 3, 100 per cent. Poor results, none, 0 per cent.

Open division of iliotibial band, 40 cases. Available for result study, 35. Good results, 30, 86 per cent. Poor results, 5, 14 per cent.

Open division of iliotibial band combined with tenotomy at the hip, 28 cases. Available for result study, 24 cases. Good results, 15 cases, 62.5 per cent. Poor results, 9 cases, 37.5 per cent.

Hip fasciotomy combined with open division of the iliotibial band, 45 cases. Available for result study, 42 cases. Good results, 37 cases, 88 per cent. Poor results, 5 cases, 12 per cent.

Total group, 160 cases. Available for result study, 150 cases. Good results, 120 cases, 80 per cent. Poor results, 30 cases, 20 per cent.

Combined figures for major procedures, 158 cases. Available for result study, 140 cases. Good results, 114 cases, 80 per cent. Poor results, 28 cases, 20 per cent.

9 Each case should be considered individually for the selection of proper procedure.

10 In view of the fact that the original causative muscle imbalance is not altered we feel that this is a high proportion of satisfactory results. Moreover, the degree of muscle loss and muscle imbalance is apparently not the determining factor in recurrence.

11 Milder deformities and young children have shown a higher percentage of recurrence than severe deformities and older children.

#### BIBLIOGRAPHY

- 1 ALBEE, FRED H. *Orthopedic and Reconstruction Surgery*. P 724. Philadelphia W B Saunders & Co, 1921.
- 2 SOUTTER, ROBERT. A new operation for hip contractures in poliomyelitis. *Boston M & S J*, 1914, 170:380.
- 3 SPEED, J S. End results in transference of the crest of the ilium for flexion contracture of the hip. *J Bone & Joint Surg*, 1928, 10:202-218.
- 4 STEINDLER, A. *A Text Book of Operative Orthopedics*. P 29. New York D Appleton & Co, 1925.
- 5 YOUNT, C C. The rôle of the tensor fasciæ femoris in certain deformities of the lower extremities. *J Bone & Joint Surg*, 1926, 8:171.



## OSTEOMYELITIS IN INFANTS

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**E**XPERIENCE with more than 300 cases of the subacute and chronic forms of osteomyelitis leads me to the conclusion that this disorder in the acute state is rarely accepted as a clinical entity by the profession, that in practically every instance it remains unrecognized and is therefore neglected in the early stage when treatment would do most to prevent unfortunate sequelae.

The same was true of appendicitis before it was recognized as a common clinical entity: a similar period of neglect elapsed, but the disease was so prevalent and the leaders in surgery continued to emphasize the characteristic symptoms until finally the syndrome has become so definite that even the average layman has come to know that if a person is seized with pain in the belly with vomiting and localization of the pain in the right lower quadrant, and with elevation of temperature, that person in all probability has an acute appendicitis and the appendix should be removed. At least it may be said that today almost every practitioner of medicine upon finding localized tenderness in McBurney's point and leucocytosis, properly advises appendectomy. Popular misinformation has even led to the expression that unless the appendix is removed the patient will die—an error of course in most instances, for there is reason to believe that in most cases, the condition would resolve.

There is little reason to expect such good fortune in the early recognition of acute osteomyelitis which though the outcome is seldom fatal, does demand, in nearly every instance, surgical interference or else the victim becomes a subject of prolonged invalidism, the duration of the invalidism being in direct ratio to the delay in the recognition of the condition in the acute stage. I believe that this disease causes as great morbidity and crippling as does tuberculosis of the joints or infantile paralysis. It is needless to point out the reasons, chief among which is error in diagnosis. This may be traceable to the fact that the disease is relatively rare in so far as a single practice is concerned, to the absence of objective phenomena, and to the negative X ray findings at the onset.

In the propaganda for reform in the handling of this malady we should enunciate a dictum analogous to that in acute appendicitis, and as teachers of surgery we should reiterate the

dictum until it is established upon a traditional basis. This dictum should be stated as follows: If a child under 15 years of age is seized with pain in an extremity and he shows loss of function, elevation of temperature and leucocytosis, that child has acute osteomyelitis. Any other entity such as acute arthritis, acute articular rheumatism, neuritis, poliomyelitis, is improbable. In such a picture the obligation of the doctor is to determine the point of localized tenderness over the end of a long bone, and, upon recognition of this point of tenderness, to open the cortex and drain. This seems axiomatic to the orthopedic surgeon of experience who seldom sees these patients until the sequelae incidental to neglect are in evidence, namely: extensive bone necrosis, multiple metastatic lesions ensuing upon the primary one—in the hip and elbow septic arthritis, fracture, and deformity—parenchymatous and cardiac lesions, secondary anemia, to say nothing of deformities due to disorders of bone growth. The dictum should be disseminated to the general practitioner.

The difficulties met in these cases are several. One is the contention of the child that the pain is in a joint when it really is not, and here we must utilize art and skill in the segregation of bone from joint. Too little stress has been laid upon the fact that a joint adjacent to a bone which is the seat of acute osteomyelitis becomes distended by effusion of fluid rich in leucocytes that looks like pus but is sterile. This leads to the diagnosis of septic arthritis and drainage, hence infection of the joint, the surgeon is lulled into a feeling of accomplishment, the real focus is neglected and great harm results. It should be remembered that in acute osteomyelitis of a vertebral body similar effusion occurs into the spinal canal and may be associated with symptoms of meningeal irritation.

Another pitfall is the disparity between the subjective phenomena and the visible or palpable finding: no swelling, no redness, negative roentgenograph, only localized tenderness and that difficult to localize. If the child is old enough and the examiner adroit the area of tenderness can be determined.

The degree of pain and the loss of function and elevation of temperature may be confusing, because it varies with the nature of the invading organism, the age of the bone involved, and the resistance of the child.

Great, indeed, are the difficulties when the child is too young to co operate in localizing the area of tenderness, and the examiner is left to more intuitive resources. Fortunately, however, delay is less injurious in the young child than to the older one. Of the greatest importance, in the child of 15 or over is the very early drainage because in such patients the traditional reliability of the epiphyseal cartilage to resist invasion to the adjacent joint has become impaired because the cartilage is thinner, at that and greater ages.

Acute osteomyelitis is a disease exclusively of children, i e., it is a hematogenous infection lodging in the end arteries and stagnant venous sinuses of the growing epiphysis. These latter do not exist in the adult bone and vary at ages in childhood. It would appear that osteomyelitis supervening in an adult is in all probability a lighting up of an ancient quiescent process acquired in childhood. The arteriovenous arrangement seems to be especially adapted to the development of infection between the ages of 5 and 11 years. Fortunately, the epiphyseal cartilage is thick at this time and is nearly always competent to prevent extension of infection to an adjacent joint, neglected disease will rupture through bone, periosteum, fascia, and even skin, and leave the joint unimpaired. However, at the upper end of the femur and the lower end of the humerus, the epiphyses and the adjacent diaphyses are inside the joint capsule of hip and elbow, respectively, hence, rupture near the epiphysis is into the joint so that septic arthritis ensues. However, even in these, direct approach to the bone lesion early, even through the joint, will save the joint.

As previously referred to, in the older child, 16 to 18 years, the epiphyseal disc is thin (bone growth having been nearly completed) and may thus enable jointward extension. It may well be stated, therefore, that acute osteomyelitis becomes progressively a more urgent and serious problem with the increased age of the patient.

In a consideration of the subject as a whole, a correlation of the pathogenesis and subsequent changes with the clinical evidences is necessary, and in our series the following facts have been driven home by repetition.

In the prevalent age

1 Boils on the skin are the most frequent primary focus, otitis media next.

2 The onset is abrupt, with pain usually in an extremity for which no sufficient cause can be assigned (although usually a history of trauma), associated with fever and leucocytosis.

3 Pain is constant and is not relieved by rest to the degree that would obtain in a joint lesion.

4 Loss of function of the extremity occurs to a curious degree, there is no muscle spasm as in a joint lesion. The extremity lies limply and movement passively is resented, although it can be done painlessly. This may readily cause confusion with poliomyelitis.

5 A joint infected cannot be moved a single bit without great pain. A joint seemingly but not really the seat of infection and near a focus of osteomyelitis can be moved passively carefully and painlessly.

6 Localized tenderness in a joint process is definitely around the edge of the articular ends of the bones. In osteomyelitis it is not there, but at the diaphyseal side of the epiphyseal cartilage.

7 Absence of those other phenomena so firmly entrenched in our minds as necessary evidences of inflammation, viz., swelling, heat, and redness, and absence of X-ray evidences. It is too early, these are all present but inside an unyielding tube—hence, not discernible.

8 In long bones of the extremities, the picture is sufficient and calls for removal of a window of bone and drainage. The prognosis is excellent. In 3 weeks general radiographic study of the whole skeleton is justified as well as clinical study for secondary foci which, because of immunization of the subject, are subacute in their evidences and hence easily overlooked.

9 The primary drainage is seldom final as bone necrosis will occur necessitating later ablation in from 8 to 12 weeks.

10 In the definitive treatment, the object to be attained is radical excision and obliteration of the defect surgically, for which no substitute, such as antiseptics, injections, or maggots will ever do.

11 Bones imbedded too deeply for palpation present a more difficult problem and may be incapable of diagnosis until X-ray evidences are available or abscess supervenes. However, in acute febrile and painful disorders of the abdomen in children, one should remember that the lesion may be somatic instead of visceral. The crest of the ileum, anterior superior spine, anterior inferior spine of the ileum, and the tuber ischi are common sites. I have seen several patients with acute osteomyelitis of the pelvic bones upon whom abdominal operations have been performed for acute appendicitis, ileus, and what not, and in the thorax, osteomyelitis of a rib with extrapleural abscess thought to be empyema thoracis.

12 In the vertebra, sacrum, and some widely disseminated lesions, one is sometimes stumped by the insolubility of the problem.



Fig. 1. Case. On admission. Osteomyelitis left femur. Not evidence of loss of function of left lower extremity.

Fig. 2. Case. On discharge.

So much with reference to the general aspects of the disorders at the common age of incidence. These remarks are prefatory to the report of cases in infants affording opportunity to contrast the manifestations therein to that at the usual ages. Someone has said that infants under 1 year are immune, and judging from the available literature on the subject, osteomyelitis is very rare in infants or else is usually overlooked altogether, and I am inclined to suspect the latter as the reason for the supposed rarity.

Indicative of the paucity of reference in the literature is the fact that a survey thereof for the last 18 years discloses few articles mentioning it,

and only 1 case of acute osteomyelitis of a long bone in an infant is definitely reported.

Wade, in an article on osteomyelitis in children, states that the incidence is from birth to 3 months, then none until 2 years, but presents no specific case in an infant.

E. Marx reports 36 cases in the maxilla seemingly associated with mastitis in the mother, impetigo, and a habit of mothers of putting their fingers in infants' mouths.

Madler reports an acute case involving the vertebrae in an infant of 3 weeks.

Baumgartner reports a case in the skull.

Karpus reports a case affecting mandible and tibia.

Pyrah and Pain, reviewing 263 cases, mention in the age incidence 6 cases under 1 year of age, but no specific reference is made to their course.

It is thought that the disease in early infancy constitutes an entity of such clearness as to set it apart from the ordinary picture at other ages.

The reports of 3 cases in infants under 6 months of age follow.

CASE. J. R. aged 6 months, as admitted to the hospital April 5, 1930. Child had been perfectly well until the age of 4 months, when almost apparent cause because fretful and irritable and developed temperature of 100 degrees F. In 3 or 4 days the left lower extremity began to droop and showed every evidence of flaccid paralysis. Pain as evident on efforts to move the extremity. Physicists regarded it as poliomyelitis. A few days later there was enlargement of the left thigh superiorly and laterally. X-ray seemed tender. Roentgenograph disclosed expansion of the upper end of the shaft of the femur. Intracortical



Fig. 3. Case. a, Note periosteal expansion of upper half of left femur and loss of normal conformation of the bone and circumscribed area of destruction in upper

end of right femur. b, Skull lesions. c, General view of trunk and extremities. Note lesions in both femora, lower end of left humerus, and opacity in mediastinum on right.



Fig. 4. Case 2. a. General increased opacity of right shaft of femur. b. Six weeks after operation. c. Two years after operation.

a. Shaft of femur. b. Six weeks after operation. c. Two years after operation.

tubercles test were negative. History of lues in both parents led to suspicion of syphilis, but appeared negative on roentgenologic examination.

The child came to the hospital 1 month after the onset. General appearance good (Fig. 1) although the left ear had continued to crackle with temperature 101° degrees. Appetite good. Physical examination through out was negative except for (1) left lower extremity which hung loosely without voluntary motion at hip or knee although the foot was elevated up a plantar surface. The left thigh was enlarged through out its length felt boggy and seemed to be tender but not greatly so. No fluctuation was elicited. Movements at hip and knee could be carried out passively gently without pain. (2) Over the left parietal aspect of the skull there was an elevation circumscribed as large in diameter as a dollar seemingly fluctuant.

**Roentgenologic study.** Figure 1 femur left. The upper one half was expanded and pear shaped with thin cortex and cavitation as in bone cyst or giant cell tumor. The upper half of shaft was evidently dissolved away and the periosteum had been elevated. The lower half of shaft appeared normal. No evidence of hip joint destruction was present. Right femur disclosed in the neck a circumscribed area of increased radiability, a cavity without periosteal reaction.

Figure 2b, 31 left. Three circumscribed areas measuring 1 centimeter in diameter simulating cystic disease were present in cortex and parietal bone anteriorly.

Figure 2c, general view of trunk. In addition to changes noted above left humerus disclosed in its lower third periosteal elevation and expansion of the bone and a cavity circumscribed in the distal end of diaphysis. The chest revealed an area of decreased radiability in the mediastinum to the right and above the cardiac shadow, evidently either hilus thickening or inflammatory process in the mediastinum.

**Other laboratory findings.** Urine, negative. Blood hemoglobin, 66 per cent, red blood cells 4,020,000, white blood cells 23,400, neutrophils, 46, lymphocytes, 50, eosinophiles or large mononuclears 2. Kolmer negative.

In the light of the multiplicity of lesions, the abrupt

onset and evidences of febrile nature with abscess, the conclusion was reached that the diagnosis of acute osteomyelitis was justified. Neoplasm was ruled out by the multiplicity of lesions and the fact that the child was not old enough for a neoplasm to have reached the size noted unless beginning before birth. Tuberculous disease might be suspected from certain X-ray aspects alone, however, no hint, other than a hematogenous infective process could fill all requirements in the diagnosis.

Apiration was done in the parietal bone swelling and no fluid secured. The left femoral mass yielded grayish yellow purulent material which upon smear and culture was negative.

**Operation.** In the light of continued elevation of temperature and leukocytosis and seeming deep fluctuation and aspirated fluid, exploration of the left femur was done. In the soft parts a small quantity of watery purulent material was evacuated and the bone was exposed at the site of expansion. The cortex was thin and softer than eggshell. A window was removed and the cavity found hollow and not trabeculated and contained a few cubic centimeters of crumbly sanguineous fluid. No sequestra were found. A small rubber wick was inserted and removed in 3 days followed by very rapid closure.

Culture and smear of fluid were negative. Bone tissue, recent periosteal bone.

The recovery was rapid and uneventful. The general nutrition rapidly improved. Temperature gradually subsided. No clinical evidence of the lesions was noted other than at the left femur which gradually subsided in swelling and resumed movements and normal contour and complete recovery to normal.

The patient had acute hematogenous osteomyelitis, the lesion became sterile and rapid restitution of damaged bones resulted. Upon discharge from the hospital June 6, 1930 less than 3 months from admission no clinical evidences remained (Fig. 3).

Roentgenograms taken recently, but not available, disclosed no abnormalities in the skeleton.

Case 2. I. W. aged 4 weeks, normal delivery. Circumcision was done at end of 1 week, no infection.



Fig. 5



Fig. 6a



Fig. 6b



Fig. 7

Fig. 5. Case 3. Appearance of left lower extremity on admission to the hospital. A fluctuating swelling over patella and general swelling of the knee with flexion are exhibited.

Fig. 6. Left knee a, Generally increased opacity of knee joint seen on roentgenogram. Patella not ossified. b, Five weeks after operation. No evidence of disease.

Fig. 7. Case 3. Four weeks after operation.

Fracture occurred on medial aspect right thigh. 1 age of weeks. Restlessness and irritability at 34 weeks, associated with loss of function of left lower extremity.

On admission to the hospital, temperature was 100 degrees. Right lower extremity lying as if paralyzed. The lower end of the leg appeared red and felt as if there was little general swelling. Pressure over the distal end of shaft on the lateral aspect over the epiphysis seemed to cause pain and as evidently the area of infection localized tenderness. Leucocytes numbered 25,000. The evidence was sufficient to enable diagnosis of acute osteomyelitis of femur. A needle as inserted at this point in the bone and few drops of thro pus were withdrawn.

A 1/2 inch 18 gauge Right thigh. General enlargement of soft parts and increased opacity from hip to knee. Small irregular area of increased radiability in the lower femoral diaphysis laterally just proximal to epiphyseal line (Fig. 4a).

Operation. At age of 4 weeks an incision was made at the lateral aspect of the lower end of the femur and small abscess was found deeply superficial to the bone. The periosteum found to be loose and elevated by pus from within. The periosteum was opened freely. The bone was not entered. One small gutta pariesi drain was inserted and hot wet dressings were applied.

There was immediate and rapid improvement. The drain was removed on week, during which time the discharge from the wound was moderate. The wound closed at the end of 3 weeks and function gradually returned, temperature subsided, and all evidences of disease disappeared within 3 weeks.

Culture of fluid disclosed *Staphylococcus aureus*.

Radiographic examination 6 weeks after operation (Fig. 4b) revealed little expansion of bone at the epiphyseal border of the diaphysis of the right femur at the lower extremity. No evidence of bone disease within. Two years later the child revealed no evidence of atrophy. Radiograph (Fig. 4c) disclosed normal bone structure with little projection of bone from the diaphysis just above the epiphysis—the remnant of the old elevation of periosteum.

Case 5. 8 M. aged 5 weeks. On admission to the hospital no history was available except that for 3 days baby had been fretful and feverish. One week before admission, child lost function of the left lower extremity which began to draw up.

Temperature as depressed. Patient was markedly anorected, irritable, skin dry. Left lower extremity was about voluntary movements. The knee was flexed above 90 degrees, and in the popliteal area, a circumscribed swelling which was hot and red and fluctuant (Fig. 5).

The knee could not be extended passively. Roentgenogram on admission (Fig. 6a) revealed no white line to marked flexion of the knee, general increased opacity of the soft structures of the joint. No definite bone pathology as evident.

A diagnosis of probable acute osteomyelitis of the patella was made.

At operation, needle was inserted into the fluctuant swelling and yielded a cubic centimeter thick yellow pus. An incision as made anteroposteriorly around the patella and a cubic centimeter of pus was evacuated. Vertical traction was applied to extend the knee.

On culture the fluid disclosed short chain streptococcus.

Drainage as profuse the knee gradually extended and all evidence of inflammatory process subsided within 4 weeks, and complete and evidently painless motion of the knee returned, with rapid healing of the wound and general improvement (Fig. 7).

On discharge 3 weeks after admission, roentgenogram (Fig. 6b) disclosed no disease except some opacity of the soft structures of the joint. The patella was not ossified sufficiently to cast shadow.

There was no indication of any intra articular process and upon the basis of the location of the lesion and the sensory source of the pain, it appeared that the focus was in the patella.

One cannot help but be impressed in these cases by the general appearance of well being in Case 1 despite numerous untreated foci of osteomyelitis, the marked degree of loss of function of the entire extremity in all of them, the rapidity of resolution upon simple drainage, and the absence of subsequent bone destruction and sequestration.

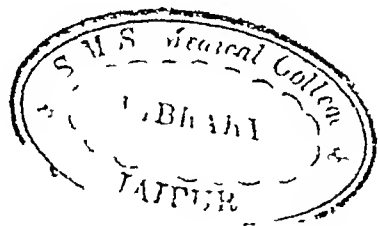
## SUMMARY AND CONCLUSIONS

1. Attention is called to the fact that acute osteomyelitis is rarely diagnosed sufficiently early to avert extensive destruction and complications.
2. Particular attention is directed to the fact that the disorder in infants is rare; at least there is a dearth of evidence that it is recognized if the number of cases is more than is supposed.
3. Three cases in infants under 6 months of age are reported, 2 of which are under 6 weeks of age.
4. The clinical picture of the disease in infants is contrasted with that in the usual age of incidence with the conclusions that:
  - a. The disease is rare in infants.
  - b. It is relatively benign and neglect to treat it in infants is less harmful than in adults.
  - c. Loss of function is singularly manifest.
  - d. Drainage alone appears to be adequate treatment.

- e. Focus of infection may become sterile.
- f. Spontaneous resolution without treatment may occur.
- g. Sequestra do not form.
- h. The prognosis is favorable.

## REFERENCES

1. BAUMGARTNER, J. Primary acute osteomyelitis in an infant's skull. *Rev. med. de la Suisse Rom.* 10: 24, 1910.
2. KATZELIS, D. Multiple osteomyelitis in an infant with only acute general symptoms. *Surg. Clin. N. America* 1931: 11, 149.
3. MANN, J. Acute vertebra osteomyelitis in a three-week infant. *N. York J.* 10: 2, 16, 1935.
4. MAX, F. Osteomyelitis affecting the upper jaw of young infant. *Nederl. Tijdschr. Geneesk.* 10: 2, 34.
5. PEARCE, F. N., and LAY, A. B. Acute infective osteomyelitis. *Brit. J. Surg.* 1931: 2, 592.
6. WAIN, K. B. Acute osteomyelitis in children. *Med. J. Australia* 10: 1, 1, 1934.



## MESENTERIC VENOUS THROMBOSIS

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**M**ESENTERIC vascular occlusion and its sequelae have occupied man's attention for three quarters of a century but nearly all published work has emphasized the arterial form of the disease, obscuring the less common venous variety. Everyone is familiar with the dramatic series of events which follows the breaking off of an embolus from the heart or aorta and its lodgment in the mesenteric artery but not everyone is aware that violent abdominal pain, ileus, and collapse may mean mesenteric vascular occlusion even though the patient have no signs of cardiovascular disease. For this reason we are presenting a new case of intestinal obstruction following thrombosis of the mesenteric vein, an analysis of 70 cases collected from the literature, and a general review of work on the subject published between 1913 and 1933.

## HISTORICAL

Interest in this subject really dates, as it does with so many, from Virchow's presentation of his first case of occlusion of the superior mesenteric artery in 847 Litten, Kärcher, Chenebisse, Gerhardt, and many others reported cases, emphasized clinical points, and experimented with this peculiar type of intestinal obstruction, and in 899 Welch and Ball published a thorough experimental study of the entire subject. Jackson, Porter, and Quinby collected all of the available cases from the literature in 1904, added 26 new cases, and made a critical analysis of all of the theoretical and practical work which had been done up to that time. Welch's section on the diseases of the blood vessels in Albarr and Rolleston's *Surgery* in 909 restated his former work with some modifications in the light of further investigations.

In 933 Trotter published his Cambridge monograph in which he brought together all the work done since 847 and reported 360 cases from his own series and from the literature. Since then the number of cases and the volume of writing on the subject has increased tremendously but we felt that the occlusions of the superior and inferior mesenteric veins should be treated separately and a review made of the present status of the disease in spite of or even because of, its clinical similarity to embolism of the mesenteric arteries.

## PATHOLOGY

The mechanism of intestinal infarction has been the subject of great controversy since the first case was reported, and even yet is not entirely solved. Exact experimental reproduction of the *in vivo* processes is almost impossible, and the results have not been too gratifying, however a fairly logical explanation is possible and the following presents a brief résumé of current opinions. That it is conducted from the standpoint of arterial occlusion does not invalidate our *in vivo* purpose of considering only venous occlusion, for the two processes are similar in their end results and the same conditions affect them both besides, only in this way can we keep any parallel to other papers written on the subject.

At first thought it would seem that infarction of the intestine should be an extremely rare occurrence because of the extensive anastomoses present in the mesentery and that when it did occur it should follow the rules laid down by Spengel that occlusion of an artery gives an ischemic infarct and occlusion of a vein a hemorrhagic one. Neither of these things is true the disease is relatively not rare and both forms of occlusion cause the hemorrhagic infarct, with very rare exceptions. It is the explaining of these paradoxes which has proved so difficult.

The superior mesenteric artery springs from the front of the aorta beneath the pancreas and rapidly divides into many branches which supply all of the small intestine and about one half of the large. Between these branches run connecting channels parallel to the bowel forming a series of from one to five arcades, depending on how far down the small intestine one goes. From the last arcade run straight vessels, the vasa recta, which arborize in the bowel wall. Older writers state that the vasa split to encircle the gut and that they anastomose with their neighbors there. Calkins' injection experiments<sup>1</sup> showed that this is not true each vessel supplies but one side of the bowel and does not connect with its companions on either side, although there is considerable overlapping of their branches. He also confirmed previous findings that the superior mesenteric artery has practically no anastomoses with other vessels, and that the veins of the mesentery

<sup>1</sup>Unfortunately in each compound as this credit cannot be given for any specific item given in this sentence.  
 The diagram of Calkins illustrates this point with great clarity.

follow the arterial distribution closely throughout except for the region supplied by the ileocolic artery where the veins do not form an ileocolic vein but are direct primary origins of the superior mesenteric vein. These observations give anatomical confirmation to Litten's statement that the superior mesenteric artery, although not strictly an end artery still behaves like one. With sudden occlusion of either the main stem of the vessel or of two or more *visa recta* blood should be cut off completely from all or a part of the bowel wall but it is not apparent why infarction should occur with occlusion of one of the intermediate branches. To explain this two other peculiarities of the bowel circulation must be taken into consideration. The pressure in the mesenteric circulation falls quite rapidly and adequate circulation through the last arcades and terminal branches is largely dependent upon impetus derived from peristaltic movements. Now one of the first responses of the intestine to interference with its oxygen supply is tonic contraction, a response which not only completes the ischemia of the part by sheer muscular pressure on the small intramural vessels but by interfering with peristalsis causes stagnation of the blood stream and induces extension of thrombosis, edema and extravasation of blood.

Thus we see that the location of an occlusion is of the greatest importance followed closely by the time factor. If a sudden closure of the main stem of the superior mesenteric artery occurs above the point where any of its branches come off, there will in all probability result an anemic infarct of the entire small bowel and part of the large bowel if the vein should be closed at this same point an hemorrhagic infarct of the same territory will follow. These lesions have been observed a few times both clinically and experimentally. A slow closure at the same point may result in infarction in temporary symptoms of pain and intestinal hemorrhage or even in no symptoms at all if the occlusion progresses slowly enough for the collateral channels to open out and carry the load. This is evidently what had happened in the oft quoted cases of Virchow and Karcher who found at autopsy the superior mesenteric artery represented by a solid fibrous cord although the patient apparently gave no history of intestinal disease.

If, now, the occlusion takes place anywhere below the splitting of the artery and above the last arcade, there are several possibilities to be considered. Ligations in this region have generally produced no symptoms at all or at most transitory ones, and in Cokkinis injections such ligations

did not prevent the injection fluid from reaching any part of the gut. If the disturbance produced in the bowel by the initial trauma is of sufficient severity, it may during prolonged tonic spasm cause either marked changes in the bowel wall or by stagnation induce secondary thrombosis in the mesenteric vessels distal to the point of initial occlusion with permanent vascular isolation of that segment. It is this latter process which Cokkinis feels is responsible for many of the infarctions following localized embolic occlusions in the middle of the mesentery. But here again if the occlusion is slow enough the spasm will never occur secondary thrombosis will not develop a rearrangement of circulation will take place, and the patient will ultimately recover (in fact may never have symptoms). Of course, with the elaborate by pass system of the mesentery back flow must occur into any such territory or in the case of the venous occlusions inflow from the arterial side and so in both cases the final lesion will be a thoroughly blood soaked hemorrhagic infarct.

Finally occlusions in the *visa recta* must cause cutting off of the blood supply to the part for there are no anastomoses beyond the terminal arcade. However there is sufficient overlap of the terminal arborizations that occlusion of one vessel will seldom if ever cause trouble, experimentally the vessels supplying about 3 centimeters of bowel must be affected before infarction occurs, and clinically the smallest lesions are of about that size.

As we stated before, much the same laws conditions and processes apply to the channels carrying blood away from the part as to the supplying arteries the only differences being the time factor and the possible occurrence of back pressure on the venous side from an obstructed portal circulation. Arterial occlusion is almost always a sudden embolic affair venous occlusion a slower thrombotic process. In this connection there is one point of great importance which we feel has not been stressed sufficiently by former writers that is, that this difference in speed of events may not be obvious clinically. The compensatory powers of the body are extraordinarily great they may be able to care for a relatively slowly failing circulation without symptoms up to a certain point, but find themselves with dramatic suddenness unable to carry on further, whereupon the typical acute symptoms will appear without warning, although the process has been going on for some time. It is of the greatest importance that the clinician realize this when he is faced with an obscure case of abdominal pain in a young, apparently healthy



person who has no right to an embolus from any cardiac or arterial source.

The pathological changes in the bowel, reported as resulting from one or another stage of this complex mechanism vary from none to complete gangrene. Edema and congestion of the small sub-mucosal vessels appear to be the earliest noticeable change followed by increasing degrees of this same process up to marked edema, congestion, petechial hemorrhages, and focal sloughing of the mucosa. The bowel is moderately dilated, dark red in color, heavy, soggy and filled with thin, bloody fecal material. Necrosis and gangrene begin at the mucosal surface and extend outward as is shown by cases reported with shelling serosa over necrotic muscle and mucosa. However such a stage is short lived. Invasion of the gut wall by intestinal bacteria beginning early and rapidly causing peritonitis. Bloody ascites, probably a transudate from the congested intestine is an almost constant finding.

#### PATHOLOGY OF REPORTED CASES<sup>1</sup>

**CASE 1.** A male, 67 years of age. The sigmoid and findings at autopsy were as follows: The peritoneal cavity contained nearly 1 liter of foal, yellowish, turbid fluid, in which are suspended large flocks of fibrin. The peritoneal surfaces were injected throughout. The entire small intestine was dilated, with dull, injected serosa and boggy wall. In the midportion of the jejunum are 10 firm, dark red bands, heavily coated with fibrin, approximately 8 centimeters in length and adjacent to one another. The arterioles of the mesenteric artery of the third order leading to these two points were occluded by small emboli. The mid portion of the transverse colon showed a similar dark red, fibrin coated swelling, again about 8 centimeters in length, and the supplying twig of the inferior mesenteric artery as occluded by an embolus. The smaller branches of the superior mesenteric vein were markedly dilated. The portal centimeters of the superior mesenteric vein itself and the immediately adjacent portions of the portal contained firm, dark red friable adherent thrombus. The liver weighed 540 grams and was markedly irregular in contour, showing an extreme degree of lobulation, with its nervous deep, furrowed scars. The color of the lobules ranged from purple to yellow. The aorta was notably calcified and distorted by atheromatous plaques, many of which are ulcerated and overlain by adherent, reddish mural thrombi. In addition, the thoracic aorta as the site of two mural aneurysms.

Microscopically the small intestine showed congestion and edema of the mucosa with polymorphonuclear infiltration and some desquamation of the lining cells and marked edema and leucocytic infiltration of the submucosa, muscularis and serosa. In addition, the dilated serosal vessels and lymphatics contained numerous polymorphonuclear leucocytes. In the reddened, more indurated portions of the intestine the same changes were noted, together with foci of hemorrhage and some intense polymorphonuclear infiltration of the tissues. The mesenteric arterioles supplying these more intensely involved foci contained occluding emboli made up of agglutinated masses of platelets with slight amount of fibrin and few red blood cells. Sections

of the mesenteric vein showed an occluding thrombus composed of fibrin, agglutinated platelets, red blood cells, and numerous polymorphonuclear leucocytes, which was adherent to considerable portions of the circumference of the vessel and displayed moderate amount of organization by ingrowth of fibroblasts from the vessel walls. In one or two sections, portions of the media of the vessel were to be necrotic and infiltrated by polymorphonuclear leucocytes. The liver showed the characteristic changes of splanchnic embolism.

**Autopsy diagnosis:** Gangrene of small intestine with associated acute generalized peritonitis, secondary to thrombosis of portal and superior mesenteric vein, splanchnic embolism of liver, embolic infarction of portions of small intestine and colon, secondary to mural thrombi of aorta. Coexistent but not immediately associated lesions include splanchnic arteritis, aneurysms of thoracic aorta, acute purulent pericarditis, acute fibrinous pleuritis, old right nephrectomy, fibrosis of islands of Langerhans.

**CASE 2.** A hit male, 53 years of age. The significant findings at autopsy are as follows: Approximately 1 liter of thin, bloody fluid lay in the abdominal cavity. There were several patches of purplish discoloration of the parietal peritoneum. The entire gastric intestinal tract as well as the small intestine showed marked distention, edema of the wall, and dark purplish discoloration. About 10 centimeters below the pylorus the jejunum was marked by a pale band approximately 1 centimeter wide. T and one half centimeters further down, the intestine was again marked by a similar band. Between these two points, the intestinal wall was dark purple, edematous, extremely friable, and coated with thin layer of fibrin. No definite points of adhesion or obstruction could be found, though there were a few old scars above between the mesentery and the mesenteric peritoneum. In the lower portion of the ileum there was a Meckel's diverticulum, 10 centimeters in diameter and 3 centimeters in length. The larger mesenteric veins contained thrombi and there was slight necrosis of some portions of the mesenteric fat.

Macroscopic examination showed extreme congestion of the jejunum, with marked edema, hemorrhage and necrosis. Moderate amounts of fibrin were present as well as some polymorphonuclear infiltration. In some sections the submucosa and portions of the muscularis showed good deal of increased connective tissue.

Throughout the sections of the intestine there was intense capillary and venous congestion. The superior mesenteric vein contained pedunculated, fibrin and platelet thrombus adherent to the wall, almost completely organized by ingrowing fibroblasts. Other vessels along the intestine made up of platelets, fibrin, and red cells, adherent to the wall, with very slight fibroblastic ingrowth. Still others were completely occluded, without organization, by masses of fibrin, platelets, and red blood cells.

**Autopsy diagnosis:** Thromboses of superior mesenteric vein and its tributaries, its gangrene of jejunum and portions of ileum. Coexistent but not associated lesions include atherosclerotic arteriosclerosis of aorta, atherosclerotic nephrosclerosis, hyalinization of islands of Langerhans.

These 2 cases serve to emphasize the diverse nature of the processes involved in mesenteric occlusion, in spite of the similarity in the ultimate results. In the first case we have a probably sudden massive thrombosis of the portal and superior mesenteric vein, precipitated by stasis in the portal circulation secondary to a

badly damaged liver, in the second, we have numerous thrombi of varying ages occurring without any discernible cause, yet in both almost exactly similar changes in the intestinal tract. What part the arterial embolism may have played in the first case is not entirely clear, but was apparently limited to local intensification of the general infarction, and was only a chance occurrence rather than related to the venous thrombosis. The age of the venous process was such as to preclude the possibility of its being secondary to infarction resulting from the arterial embolism, as we have clear cut evidence of some days' duration of the venous thrombosis afforded by partial organization of the thrombus. In our second case we have no known cause for the initial venous thrombosis, but the nearly completely organized thrombus in the superior mesenteric vein, once formed, would have produced marked stasis in the portal circulation and given a basis for the formation of subsequent thromboses. Variation in the time of occurrence of these is easily understood when the diverse factors of venous obstruction and of distention and necrosis of the intestine resulting from impaired circulation are considered. Once the venous return is completely occluded, the changes in the intestine can progress only to hemorrhagic infarction. Since this type of infarction usually also occurs, as we have already pointed out, in arterial occlusion, careful dissection of the mesenteric vessels is essential to establish the nature of the circulatory disturbance.

#### ETIOLOGY

The etiology of venous thrombosis in the mesentery offers the same problems as thrombosis elsewhere in the body, and probably includes an even greater number of causative factors than in most other locations. As Eliot says, "In a very considerable proportion of cases, no adequate cause can be discovered. That cases of mesenteric thrombosis not infrequently occur without discoverable cause and in patients with no history of previous illness cannot be too strongly emphasized. While the etiological importance—(of certain diseases)—must always be recognized, the fact that, occasionally, not one can be identified must not be overlooked and must not lead to the positive exclusion of mesenteric thrombosis in the diagnosis of acute and subacute obscure abdominal conditions." However, Larson, Reich, Eliot himself, and many others have shown in recent articles that there are several predisposing conditions the existence of which, along with symptoms of "acute or subacute obscure abdominal" distress, should always make one consider the possi-

bility of serious circulatory damage to the bowel. These may be grouped roughly into four major groups: infectious, hematogenous, traumatic, and mechanical.

We do not agree with the customary division into two classes of primary and secondary thrombosis, for the so called primary cases are generally those for which no cause can be found, this does not justify their being classed as primary thromboses to the exclusion of those with definite, traceable etiology. It seems more logical to us to take those cases with known causes, classify those causes, and then admit that there are other cases of unknown etiology, the origin of which may or may not lie within the mesentery itself, and lump them together in a limbo of obscure cases.

Specifically, our first group includes all those cases in which there is a known infection in the region drained by the mesenteric, venous, or lymphatic system, in neighboring loci from which direct mechanical extension of the infection to the mesenteric vascular tree would be possible, or in which general circulatory sepsis exists. We do not agree with Bucura's attempt to include as infectious various hypothetical "toxic" substances present in eclampsia, leiomyoma uteri, normal puerperium, etc. Until definite evidence can be produced, as it has not been so far, that there are such substances which change the nature of the vessel wall in such a way as to induce thrombosis, we see no reason for assuming their existence while there are other factors which can equally well explain the process. We do include in the first group thrombophlebitis, appendicitis, pelvic abscesses, peritonitis, and general sepsis. The second group, that of hematogenous causation, includes blood diseases or changes known to predispose to thrombosis, such as the splenic anemias, and polycythemia vera. The third group, the traumatic, includes thrombosis from any sort of trauma to the mesenteric vessels, tearing of the mesentery, and trauma from abdominal operations. The fourth group, that of the mechanical causes, is rather large, comprising portal stasis, pressure from tumors, and pressure from adhesions or congenital bands across the mesenteric vessels. Relying principally on Moloschin's report of a case in which the occlusion was caused by tumor cells from a liver carcinoma, Reich includes retrograde embolus as a mechanical cause, but his evidence for the occurrence of such a phenomenon we feel to be weak. The cases which he supposes to have such a cause could equally well represent multiple thromboses based on sepsis or mechanical stasis. Because of obvious factors, cases of volvulus and strangulated hernias

TABLE I—CAUSES OF VENOUS  
MESENTERIC THROMBOSIS

	Warren and Cher-hod	Larson	Calkins	Black- burn	Total
Appendicitis			11		11
Ectasia					
Thrombophlebitis, Rec. and Sim.					
Endophlebitis obliterans					
Ulcerative colitis					
Dysenteria					
Alacasia					
Polycythemia	1				
Splenic anoxia and splenectomy					
Hemophilia					
Previous pelvic operations					
Pregnancy Abortion Delivery					
Pneumia Tuberculosis nodes Adenoma					
Acute leukocytosis					
Trauma					1
Phlebotomy					
Constipation					
Congestion of liver					
Partial thrombosis			11		11
Carcinoma of stomach					
Local scar of liver					
Unknown	23		11		34

have not been included in the category of essential mesenteric thromboses.

In Table I will be found a tabulation of the causes and number of cases attributed to each cause in several series collected since 1913. The table shows considerable differences in the relative frequency of various causes as compiled by different authors, but this is to be expected in such limited lists of cases of a disease with so many possible etiological agents. Perhaps the fairest idea is conveyed by the last column, in which the results of four investigators are combined. The largest group by far is the unknown and perhaps it should be even bigger for the etiological relationship of many of these conditions is open to legitimate question. For example how long may a femoral phlebitis be dormant and still hold its place as the source of the later mesenteric thrombosis? After all, there may well be a common unknown cause for both. "Previous pel-

vic operations" was included because of its occurrence in 17 per cent of our female cases, although in only 2 of these was the thrombosis an immediate postoperative complication but, in the absence of any other exciting cause it was felt worth while to mention the possibility of its etiological relationship. In the 3 splenectomy cases, the extension of the thrombosis in the ligated splenic artery was probably the real cause rather than an underlying blood condition. Calkins and Larson consider appendicitis of first importance, while Elsberg and Schlink, and Eliot and Jameson believe that portal thrombosis or cirrhosis of the liver should occupy the honor position. From our investigations we believe that septic abdominal conditions such as appendicitis and pelvic inflammatory disease probably actually account for the greatest number of cases, for many of these probably pass as postoperative ileus or peritonitis and do not find their way into the literature. Next in importance come the cases with hepatic cirrhosis, most of them fatal, nearly all of them discovered at autopsy and hence, by their very character, forcing themselves on one's attention and so coming to occupy a disproportionately large place among the case reports. One of the most important correlations in the list is that between polycythemia and mesenteric thromboses, Kratzel and Jacobl both believing that nearly all cases of the former ultimately die of the latter. Gore suggests that many postoperative patients who exhibit "pseudo-obstruction—a spasm lasting for a few hours or longer and then go on to recovery are really victims of minor mesenteric thromboses.

At the end of the table is one case which unfortunately had no clinical data to earn it a place in our general series, but as a pathological curiosity deserves mention. This, reported by Weidman, is that of a mesenteric thrombosis following breaking down of a pyemia in the right lobe of the liver and abscess formation with thrombosis of the portal and mesenteric veins.

These, of course, still do not represent all of the possible causes of thrombosis of the mesenteric veins, but only give some of the more common predisposing conditions for which the alert clinician will search when confronted with a patient with acute abdominal pain or symptoms of acute intestinal obstruction without obvious mechanical cause.

#### STATISTICAL ANALYSIS

Any statistical study of this subject must of necessity be open to almost every conceivable error that can beset a numerical analysis of a clinical subject. To gather a group of cases large enough to justify any analysis one must resort, as

TABLE II—VASCULAR LESIONS OF INTESTINAL VESSELS

No	Age	Sex	Location of infarction	Artery	Vein	Embolism	Thrombosis	Cause
156	73	F	Jejunum and ileum	+			+	Mechanical (carcinoma)
2760	67	M	Two portions 8 cm jejunum 1 portion colon	(+)	Portal, mesenteric	(+)	+	Cirrhosis of liver
5735	77	M	180 cm ileum	+		+		Aortic mural thrombi
5917	52	F	125 cm jejunum	+			+	Mechanical (carcinoma)
6327	60	M	25 cm ileum	+			+	
15079	73	F	Jejunum and ileum	+		+		
16537	51	M	250 cm ileum		+		+	
17697	71	F	Jejunum and ileum	+		+		Heart
18168	64	F	Jejunum mesentery and ileum	+		+		Heart
18359	72	F	Ascending colon	+		+		Heart
18557	69	M	Jejunum and ileum	+		+		Aorta

this country at least, to the collecting of cases from the literature, and immediately he is faced by the facts that nearly all of the histories are incomplete, there is no standard of observation, interpretation, or treatment, inaccuracies and omissions may exist in the reports, and there are not even definite criteria of what constitutes the clinical entity of essential mesenteric venous occlusion.

Cokkinis obviated some of these failings by taking his material from the records of two very large, old, reputable institutions, and from the private records of men whose ability he knew personally. He was fortunate in being able to unearth as many cases as he did, we miss statistical correlation. Larson's, Ophuels', and Ceelen's reports are excellent but comprise only autopsy material, thus giving no idea of incidence in a general population, mortality rates, or the relative value of different methods of treatment. Robey could not supply the omissions in the records of the Boston City Hospital and thus lost much data which would have been of value. In general, among the individual case reports, Cokkinis is probably right in feeling that the dramatic, successful cases stand a far greater chance of being reported than the obscure, prosaic cases which die without benefit of autopsy or operation, although the latter group undoubtedly forms a large proportion of the instances of this disease.

In Table II we summarize the mesenteric occlusions, both arterial and venous, included in the admissions to the New England Baptist and New England Deaconess Hospitals from 1928 to 1933 inclusive and to the Palmer Memorial Hospital from July, 1927, to January, 1934. The number of cases of vascular occlusion, surgical specimens,

and autopsies are taken from the records of the William L. Shearer Pathological Laboratory, through which passes all of the pathological material from the hospitals mentioned, along with a very small percentage of work from other sources.

We have listed in the parallel columns of Table III the general statistical findings of 12 series reported since 1913. The first column is based on Table II. The second column presents the figures gathered by Robey covering a 33 year period. In column 3 are Flynn's results of a 5 year period at the Baylor Hospital. Ophuels', Larson's, and Ceelen's statistics in columns 4, 5 and 6 represent studies on consecutive autopsy series. Cokkinis' figures in column 7 cover a period of 25 years at the London and Guy's Hospitals. Brady's 12 cases shown in column 9 were found at the Johns Hopkins Hospital, while Reich's, L. Miller's, and W. Smith's series consists of cases gathered from the literature with the addition of a few new cases.

The general incidence of venous mesenteric thrombosis is extremely hard to calculate because of the rarity of the disease and the paucity of figures. According to what data we could gather, it is in the neighborhood of 0.003 per cent of the general hospital population and 0.05 per cent of the autopsy populations. Table IV shows the exact figures in the seven available series. Robey, unfortunately, does not give in his paper accurate figures on the occurrence of venous and arterial occlusions, saying, "In our autopsy records there is some differentiation between occlusion of a mesenteric artery and vein, but the former far outnumber the latter." However, although only 5 of his cases are definitely diag-

TABLE III—INCIDENCE OF MESENTERIC OCCLUSION

	Warren and Liberman	Roby and May (St. Mary's Hospital)	Boyle (St. Mary's Hospital)	Ogilvie	Larson	Cook	Cobb (St. Mary's)	Reck	Reidy	L. J. McGee	W. Smith	Deaconess Hospital
Incidence	27%		29.6%									20%
Surgical intervention	24%	20.5%	27.5%									
Medical or no action	24.5%	14.5%	19%									
Mesenteric obstruction				20	24		77	25		20	45	
Mesenteric artery	6.7%		30%	60%	55%	60%	5%	45%	30%	60%	85%	
Mesenteric vein	1%	2	24%	12%	5%	60%	75%	55%	30%	30%	5%	
Surgical specimens	24.5%											
Autopsy	20.5%			2000	3000	521						
Mortality (fatal)		9.5%		600%	700%	600%			5%			
Mortality (operative)		71.7%					5%	20.5%	5.5%			
Mortality (with operation)							55%					

Table Memorial Hospital—1913-1914 inclusive

New England Hospital and New England Deaconess Hospital 1915-1916

1917-1918 inclusive—5 cases not classified

1919-1920 inclusive

1921-1922 inclusive

TABLE IV—INCIDENCE OF MESENTERIC THROMBOSIS

		W. E. G.	Thom	Ogilvie	Larson	Cook	Reidy	Reck
Venous	(H. Hospital population)	24.5%	20%					20%
	Autopsy population	19%		55	644	82		
Arterial	(H. Hospital population)	24.5%	20%					
	Autopsy population			666	89	82		
Both	(H. Hospital population)	20%					20	

known as venous occlusion there are 25 unclassified cases, 13 of which we feel may very well have been venous in character. When the general knowledge of a disease is so poor that a man of as wide experience as Dea or could make this statement in 1929, "Thrombosis of mesenteric arteries may lead to acute symptoms resembling those of acute obstruction, while a venous thrombosis will mimic the more chronic type of obstruction. Very few cases are reported in the literature those that are described were diagnosed at laparotomy and all of them were fatal—then such a man could speak thus to a state medical convention without contradiction or comment, then most men are not looking for the disease and many cases must pass unrecognized, so probably the actual incidence is far higher than these figures indicate.

As to the relative incidence of the arterial and venous forms of the disease Tables III and IV show what wide disagreement exists. Our own figures are undoubtedly misleading because of the very heavy weighting of our material with the diabetic and cardiac patients who form a large

percentage of the patients at the Deaconess Hospital. Cobb's figures are startling but considerable importance must be attached to them because of the way the cases were collected from which these results were calculated. If our supposition about Roby's figures is true his venous occlusions would nearly equal his arterials. We may safely say that the relative incidence of venous thrombosis is far higher than we supposed it to be when we embarked on this investigation.

In Table V the age incidence of venous occlusion is presented. No exactly comparable table could be presented because all other authors have computed their results with all types of mesenteric occlusion lumped together but the results agree quite well in placing the disease among those of early and middle life, atherosclerosis and cardiac failure forcing the combined tables slightly higher than our series from the literature. The youngest patient we found on record was reported in the monograph of Jackson Porter and Ounby an infant 4 weeks old. Of our cases of known age 44 per cent were under 40.

TABLE V —AGE INCIDENCE OF VENOUS  
MESENTERIC OCCLUSION

Years	Cases
0 to 9	2
10 to 19	4
20 to 29	13
30 to 39	12
40 to 49	14
50 to 59	15
60 to 69	10
Unknown	5

TABLE VI —MORTALITY

	Cases	Alive	Dead	Per cent Mortality
Total number of cases	75	31	44	58.8
Operative cases	55	30	25	45.4
Resection cases	38	25	13	34.2
Cases not operated on	20	1	19	95.0

The disease seems to occur with about equal frequency in both sexes, 52.7 per cent of our cases being male, 45.9 per cent female, and 1 case unspecified, but it appears to favor the white race overwhelmingly, all but 2 of our cases being definitely white, 1 negro, and 1 may have been Chinese. This probably merely reflects the hospital populations.

Table VI presents the mortality statistics with some results of treatment. Of the 75 cases reported, 44, or 58.8 per cent, died. Fifty-five were operated on for the lesion and of these only 45.4 per cent succumbed. Thirty-eight were subjected to resection with a mortality of 34.2 per cent. Phrased differently, 31 of the original 75 survived, and of these 30 were operated upon and 25, or 80.6 per cent, had resection. Of the 20 not operated upon, only 1 left the hospital alive.

The effect of more general recognition of the disease, of improved technique in abdominal surgery, and of better recognition of the fact that surgery offers almost the only hope of life that these patients have is well illustrated by a comparison of the general mortality compiled at approximately 10 year intervals. Cokkinis' total figure given here does not give a true representation of the facts because it includes cases back as far as 1900, whereas it is generally recognized that the major improvements have come in the last 15 years.

The tabulation of mortality in relation to the duration of symptoms is extremely misleading because of several factors. The most important one is the characteristic of the disease to proceed with moderate or no symptoms before appearing in full blown form, thus making it often impossible to state the true duration of the disease. We tried to figure in each case the time between the first appearance of really acute symptoms and operation or death, but in many could come to no con-

TABLE VII —COMPARATIVE MORTALITY

Author	Period covered	Per cent Mor- tality
Jackson, Porter, and Quinby	1874-1904	92
Trotter	?1874-1913	78
Cokkinis	1900-1926	83
Warren and Eberhard	1913-1933	58.8

TABLE VIII —DURATION OF SYMPTOMS  
AND MORTALITY

Duration	Cases	Mortality Per cent
0-12 hours	4	25.0
13-24 hours	12	41.6
25-48 hours	9	71.4
3 days	6	33.3
4 days	6	83.3
Above 4 days	16	78.6

clusion at all. Also, the extent of the pathology found may bear no relation to the apparent duration for symptoms, that is, in 1 case patient may have had symptoms for weeks and show relatively little pathological change while another patient who has had symptoms for only a day may show necrosis of the entire bowel. However, from Table VIII and the findings of Cokkinis, Reich, Elot and Jameson, Larson, Klein, and others, we may say that after the onset of symptoms of intestinal obstruction every hour of delay lowers the patient's chances of recovery. The low figure for 3 days is probably a chance finding dependent upon the chances of such small series, though it may indicate a very slight difference between the fulminating and more chronic types of cases, but this is unlikely.

McIver's monograph on intestinal obstruction brings out several interesting points in this connection. He collected 10 cases of mesenteric obstruction in 335 cases of intestinal obstruction at the Massachusetts General Hospital, studied the relation of interference with circulation to the seriousness of all types of obstructions, and found that such interference raised the mortality from 37 per cent to 53 per cent. He states "—the most important factor governing the pathology and symptomatology, and largely determining the severity of the illness is, paradoxically enough, not the blockage of the intestinal stream but the condition of the circulation to the involved segment of bowel." A case in point is that of Guibal, a strangulation of a scrotal hernia involving several loops of bowel but exhibiting its serious pathology in a thrombosis of several mesenteric veins and infarction of a portion of bowel which apparently was not included in the sac and failing to show any mechanical obstruction of the lumen of the bowel.

## SYMPTOMS AND DIAGNOSIS

In 1913, Reich made an exhaustive analysis of the symptoms of occlusion of the mesenteric vessels and worked out an elaborate classification of types of the disease. This has been repeated and modified by numerous writers notably Elliot and Jameson, Klein, and Wulsten but while interesting from a statistical and theoretical point of view does not seem to us to accomplish the primary purpose of such work—that is the clarification of a symptom complex for the benefit of the clinician. Reich believes, as do Loop and others, that there is a definite syndrome aside from the obstructive and peritonitic picture but becomes involved in technical niceties which confuse the picture from a practical standpoint. Ross goes farthest the other way and says, "The symptoms of mesenteric thrombosis, in so far as they may be grouped are those of acute intestinal obstruction. Essentially we are inclined to agree with him, although there are several special features which if properly evaluated should help to eliminate the ordinary mechanical obstructions and to point the way to a correct diagnosis and a more accurate prognosis. Cocklin believes the disease to be diagnosable in about 60 per cent of the cases and states rather forcibly "—the prognosis and results of treatment will only improve when mesenteric occlusion comes to occupy the important position it deserves in surgery, and its clinical manifestations become sufficiently well known to make early diagnosis possible.

Pain is the presenting symptom in nearly all cases, and previous attacks of abdominal pain, with or without vomiting may be of great significance. It may be localized or general and if localized may be in any portion of the abdomen. Early in the disease it is apt to be intermittent or colic like in character later becoming rhythmic, and finally merging into the steady constant pain of peritonitis. It may also migrate, confusion with appendicitis having often occurred because of the appearance of pain in the epigastrium or around the umbilicus with a later movement to the right lower quadrant. The onset is usually sudden and very severe though there may be premonitory mild, transient pain before the acute crisis. In a certain number of cases, as in our first case seen in retrospect, these earlier pains may be recognized as representing mild attacks which did not result in sufficient disturbance of circulation to cause obstruction.

Preceding, accompanying, or following the onset of pain there may be vomiting, at first reflex, later obstructive, and finally fecal or bloody. Fecal vomiting is regarded as rare by most

writers, though it was stated as being present in five of our cases, but it is always a serious and late sign and one of very bad prognostic import. Hematemesis is somewhat more common, occurring in about 10 per cent of the cases reported. It is considered a highly valuable diagnostic point and of some value prognostically, for it generally occurs rather late and is apt to indicate a lesion high in the jejunum large in extent, and not amenable to treatment. It may consist of bright red blood, "coffee grounds vomitus," or may be determined only by the chemical tests.

Neither constipation nor diarrhea can be said to be characteristic of the disease, sometimes one, sometimes another occasionally neither appearing and often both occurring at different stages of the attack. Cocklin goes so far as to say that, as in carcinoma of the bowel "any alteration in the normal action of the bowels is important. He also believes the enema to be of great diagnostic value particularly in the cases with constipation where a high enema can wash down what a paralyzed bowel cannot move and then will show blood which otherwise would not have been discovered. All writers consider melena a diagnostic point in differentiating between those obstructions with interference to the circulation and those without, again a valuable prognostic help. Strikingly little mention is made of the character of the stool in the case reports which we collected, so that we are unable to draw any conclusions as to its frequency from our own series but it is generally stated to occur in about 50 per cent of the cases, and Cocklin believes that with the more general use of the diagnostic enema this percentage would be considerably increased.

Obtention occurs early or late in about one-half of the cases and may involve only the upper or lower half of the abdomen.

The temperature is generally normal or subnormal, being at first the temperature of shock, but later when gangrene and peritonitis set in it will, of course rise in response to the infection. The pulse is more likely to be slightly elevated early and will generally be weak and irregular in character in contradistinction to the full, bounding pulse of early febrile conditions. However there may be little or no alteration in either pulse or temperature for some time, but the white blood count will nearly always give the lie to their apparent lack of response. Marked leucocytosis, averaging from 15,000 to 20,000 and often rising to 25,000 or 30,000, is one of the outstanding features of the disease, a white count out of all proportion generally to the apparent severity of the illness. Later the picture changes to the usual

complex of peritonitis with marked shock. And, finally, one of the most frightening aspects is the great speed with which many of these patients go on to death, in one of our cases the patient was dead within 3 hours of the appearance of the initial symptoms.

To repeat, sudden, severe abdominal pain, accompanied possibly by vomiting, with diarrhea or sudden constipation, shock, subnormal temperature, a high leucocytosis, possibly with blood in the stools, and with diligent search presenting a predisposing cause, should always make the clinician include thrombosis of the mesenteric vessels among his possible diagnoses. We use the word vessels here advisedly because, after all, a differential diagnosis between occlusion of the veins and arteries is highly speculative in the majority of cases.

#### PROGNOSIS AND TREATMENT

Of prognosis and treatment, relatively little need be said. The figures in Table VIII speak for themselves. If the disease is diagnosed early, and operation performed with resection of the involved bowel and its mesentery, the prognosis is relatively good but falls rapidly with every hour of delay until, after 24 hours of acute symptoms, the outlook becomes extremely bad. We do not say hopeless, for such an attitude, which was that adopted in the first case which came to our attention, results usually in nothing being attempted for the benefit of the patient, thus depriving him of whatever chances of recovery he may have had. In 5 cases in our series which recovered, the patient is definitely described as being in "shock" or in "very bad condition" at the time of operation, further facts which incline us to the belief that when dealing with a condition which is known to be almost uniformly fatal without operative interference, the only course is to give the patient whatever chance an operation may offer.

Considerable controversy raged at one time around what type of operation should be performed, but the consensus today seems to be that so long as the infarcted bowel and its obstructed blood supply are removed, it makes very little difference what type of procedure is used. Anastomosis done at the time or later seems to give equally good results, and the surgeon's judgment of the individual case must suffice. Hartglass mentions the one exception to resection which we believe to be justified when he refers to a rare type of case in which the mesentery is infarcted but the bowel is already getting adequate circulation from collateral sources, he urges careful investigation of every case in which the bowel looks to be in

good condition, because in this type of case only the necrotic mesentery need be resected. Obviously great care must be exercised not only to be sure that the case is not an ordinary one in too early a stage to show bowel changes and that the bowel is really receiving circulation from other sources, but also care must be used in resecting the mesentery not to interfere with those channels.

The extent of the infarcted bowel also seems to be of secondary importance, for death is reported when only a few centimeters are involved, while Wulsten reports, and quotes Doerfler as also reporting, a case in which the patient recovered after resection of all but a few centimeters of upper jejunum and terminal ileum. The important thing is not how much bowel is removed, but how necrotic it is and how long the patient has had to endure both the obstruction and the presence of toxic necrotic tissue. Parker emphasizes very strongly that the surgeon must not be niggardly in the amount he resects, but must go far enough into apparently healthy bowel and mesentery to be sure that he is well beyond any region of incipient involvement, a task often requiring no little courage.

#### CASE REPORTS

CASE 1 P R., white male, age 67 years, was admitted under the care of Drs F Gorham, Brigham, and F H Lahey to the New England Deaconess Hospital September 14, 1928, complaining of diarrhea and pain in region of the anus. For 1 week, 3 weeks before admission, he had had severe diarrhea, with 10 to 12 movements daily. For the next 3 or 4 days he was completely constipated and then had 3 to 4 movements a day, his usual number. Ten days before admission one movement consisted of pure, fresh blood. Two days before admission he had definite chills and for the past month had been somewhat feverish, with a highest recorded temperature of 102.4 degrees F. Physical examination showed a well developed, obese, white male. The large, fatty abdomen was slightly distended but not tender. Proctoscopic examination revealed bloody stools and a negative mucosa. X-ray examination with the aid of barium enema and a gastro-intestinal series proved negative. The urine showed a few red blood cells and many white blood cells. There was a slight amount of both sugar and albumin. The white blood count was 22,500, temperature 100 degrees F, pulse 120, respiration 22. All stools contained blood. Wassermann reaction was negative. On the fourth day temperature rose to 101.6 degrees F and patient became jaundiced. He had no definite pain but marked weakness and sweating, with vague abdominal distress. Subsequently the chest showed evidence of consolidation. Pulse rose to 180 and patient died 18 days after admission. Chief anatomical diagnoses: thrombosis of portal and mesenteric veins, syphilitic cirrhosis of liver.

CASE 2 S W., white male, age 51 years, was admitted under the care of Dr F H Lahey to the New England Deaconess Hospital about noon of July 28, 1932, as an emergency case. He had had severe abdominal pain for about 6 days, sudden in onset, originating high in the epigastrium, and cramping in character. The pain had continued without much change in intensity or location. Constipation had been almost complete since the onset of the pain, the patient having had only one bowel movement



and passing only small amount of gas. He had not vomited until the day before admission and then only once. On the day of admission he had developed considerable pain in the left lower quadrant.

The past history showed that he had never been constipated before, but had had occasional attacks of severe epigastric pain over a period of about 6 months. These attacks had not been related to meals. Last attack had been on July 4, and had equalled the present attack in severity but had cleared up spontaneously in short time.

Physical examination revealed well developed and well nourished man, exhausted and dyspneic on movement. The skin was cold and clammy and the pulse fast and thready. His abdomen was markedly distended, markedly tender over the epigastrium and left lower quadrant and slightly tender over entire left side but without rigidity. Rectal examination revealed tender mass high on the left side of the pelvis. Blood pressure was 90/80, white blood cells, 14,000, blood sugar 3 g milligrams per two cubic centimeters, urinary sugar 3 per cent, temperature, 98 degrees F., pulse, 80, respiration, 20.

The discharge notes state, "He was obviously inoperable in his present condition. He was given intravenous 10 per cent glucose balanced by insulin and later placed on continuous venoclysis of 3 per cent glucose balanced by insulin. He became rapidly worse, however. His temperature, pulse, and respiration rose to 43 degrees F., 80, and 35, respectively and he died on the morning of July 29, 1932. The pathological findings have already been considered. Chief anatomical diagnosis: thromboses of superior mesenteric vein and its tributaries.

#### CASE REPORTS FROM LITERATURE

**Case 1.** White male, aged 63 years. On the 14th patient took alcohol and oil hepatica. He had loose stools next morning. At 5 p.m. he had "tarry" stool, great pain in abdomen, and collapsed. He was seen at 8 p.m. of "the 16th." He had had obstipation for 48 hours, vomiting had been bilious at first and later fecal. Temperature was 98 degrees pulse, 80. Pain was most intense at and below the umbilicus. He was operated upon and 5 feet of small intestine was resected. The veins were thrombosed. Patient died 12 hours.

**Case 2.** White female, aged 33 years, was admitted to the hospital for an intestinal appendix. Thirty hours later she developed signs of obstruction and operation after another 24 hours showed infarction of the ileum for a distance of 4 feet. The veins from the appendiceal stump were found to be thrombosed at autopsy.

**Case 3.** White female, aged 55 years. Patient had had pelvic laparotomy year before. Following this she had some of biliousness after meals. Two weeks before admission this became much worse. On the morning of May 7 she had small bowel movement. In the evening she was seized with sudden cramps, took some purgatives and vomited, and rapidly became worse. She was operated upon 10 hours after onset of pain. At this time, the abdomen was distended and tender over the lower half, and the patient as experiencing severe nausea and griping pain. At operation an adhesion was found passing on the outer side of the mesentery causing sharp kink in the meso-ileo-fifty-fifteen inches was resected and the veins were found to be thrombosed. Patient made complete recovery.

**Case 4.** Smith, J. F. White male, aged 54 years, was seized with sudden severe pain and for next 2 or 3 days vomited dark brown material and had dark colored, watery stools. He was seen after 3 days and had some abdominal rigidity, distention and dullness in the flanks. Temperature was 100 degrees pulse, 80. At operation, large amount of bloody fluid was found in the abdominal cavity but there was no

obvious occlusion. The process was found to involve 3 or 4 feet of the lower small bowel, and several veins were thrombosed. Patient died immediately after operation.

**Case 5.** Mitchell, White female, aged 30 years. Patient was healthy athletic girl. She was seen April 3, 1932. The past history was irrelevant. She had been somewhat chafing the day before and stopping that morning. She was seized with sudden, violent epigastric pain at 2 p.m. The pain became worse and vomiting set in. The pain and nausea continued through the night. Temperature was 98 degrees, pulse, 72. No tenderness or rigidity was noted. Emetics gave normal movement and much relief. The next morning the abdomen was quite flat but not tender. A mass was felt above the pubis. Pulse rose to 80. She was operated upon 1 1/2 p.m. The abdomen contained large amount of bloody fluid. One coil of ileum 18 inches from the ileocecal valve was infarcted along the corresponding mesentery. No pulsation was felt in the vessels. The line of demarcation was sharp at both ends. Resection and lateral anastomosis were done. Patient recovered.

**Case 6.** Whitman, White male, aged 64 years. There had been "venous spasm" with inflammation and ulceration for 16 years. Thrombophlebitis of left leg, 14 years. Four days before admission he was seized with sudden pain in the abdomen. He did not vomit but there was slight distention. The belly was tense and showed diffuse tenderness—worse below the umbilicus. The last bowel movement was 3 days before. There were no peristaltic sounds. Temperature was 98.5 degrees C.; pulse, 80. Diagnosis: mesenteric thrombosis, secondary to appendicitis. General peritonitis. At bloody clots were found at operation; gut was distended, dark red, and covered with fibrin. The entire jejunum and ileum were resected and side-to-side anastomosis was done. The result was ultimate recovery and survival with permanent stoma by mouth. A segment of the small bowel, about 3 1/2 meters long, showed hemorrhagic infarction and venous thrombosis.

**Case 7.** Jacobs, Case. White male, aged 59 years. The past and family history was negative. Patient suffered an injury to the right leg, in February 9. The wound healed, but in November, 9, a thrombophlebitis of the right leg appeared. He had relapse with fever, April 5. Intestinal symptoms were noted June 5, with diarrhea and later dysentery. Death occurred on July 7, with symptoms of peritonitis and intestinal obstruction.

**Autopsy.** Clinical diagnosis—sigmoid carcinoma. The abdomen contained one-half liter of thick blood. There were hemorrhagic infarcts of the transverse colon, the tip of the mesentery and the ileocecal. A loop of gut was stuck together with pus pockets between. There were many adhesions. Gray green but glistening discolored of the ascending colon and small and large intestine was noted. Thrombi noted in the middle veins of the mesentery were adherent to the walls, thrombi were also noted in the mesocolon of the transverse and sigmoid colons. The middle mesenteric and superior mesocolic veins were thrombosed. The splenic vein was free. The right femoral and popliteal veins were obliterated.

Anatomical diagnosis: localized peritonitis with bleeding in abdomen following hemorrhagic infarct of small and large intestines. Thromboses of meso-ascending branch of the small and large intestines. Increase of red blood cells, total blood volume with splenomegaly. Red bone marrow. Old healed mesenteric thromboses of veins of right leg.

**Case 8.** Jacobs, Case. White male, aged 30 years. Patient had always been healthy. Fourteen days before admission he was suddenly seized with stoppage of feces and urine, with pain in the left upper quadrant. He became progressively worse with vomiting, wasting, and in 10 colored

The pulse was imperceptible, breathing spasmodic, belly distended, tympanitic above and dull at sides. Blood was present in the rectum. There was general abdominal tenderness and no peristaltic sound, no rigidity. Patient died February 21, 1927, 15 minutes after arriving at clinic.

Autopsy: clinical diagnosis—ileus or perforation.

Eight hundred cubic centimeters of bloody fluid was noted in the abdomen. The upper third of the small intestine was blood soaked and swollen. The spleen was large, adherent, the cut surface red, bulging, without normal architecture, and contained an infarct the size of a grain of corn. The splenic vein, portal vein, and the veins of the mesentery and omentum were thrombosed. The arteries were free. The intestinal wall and mucous membranes were swollen, blood soaked, and sloughing. The marrow of the femur was red and solid.

Diagnosis: polycythemia rubra splenomegaly with infarct, thrombosis of mesenteric veins, and hepatic veins, hemorrhagic ascites.

9. Obadalek. White male, aged 12½ years. The past history was negative. Seven days before admission he was seized with severe abdominal pain and chills. He improved after 3 days and went to school. The day of admission he was seized again while eating, by severe pain, chills, and vomiting. The last stool and passage of gas was 2 days before admission. Physical examination revealed abdominal facies, tongue, dry, pulse, weak. The abdomen was distended and tympanitic, worse above the umbilicus. Board like spasm and diffuse tenderness were noted in both lower quadrants, worse on right. There was a shifting dullness in the flanks. Temperature was 38.8 degrees C., white blood cells, 9800, polymorphonuclears, 85 per cent, no eosinophils. Diagnosis: appendiceal peritonitis. At operation 500 cubic centimeters of free fluid was found in the abdomen—serosanguineous, with clots. The jejunum was distended, dark blue in color, and the serosa was studded with petechiae. The mesentery of this part of the gut was 1 centimeter thick, edematous, pitted on pressure, and was shot through with hemorrhages which merged into a general hematoma at the base of the mesentery. The mesenteric lymph nodes were palpable. Transition was sudden. The contents of the bowel were seen through the wall as bloody fluid, and masses of *Ascaris lumbricoides* were seen in all parts of the bowel. Appendectomy was done. Patient was discharged well after 18 days.

10. Winters and Anderson. White male, aged 35 years. Patient had been in the hospital for hemiplegia. He was seen at 9 a.m. when he was feeling ill, respirations were faint, and shallow, his expression anxious and his skin moist. Pain was diffuse and the abdomen was slightly distended and rigid. The temperature was 100.6 degrees, pulse, 130 and weak. He was seen again at 12.15 p.m. in extremis. The pulse was 150 and irregular. Respiration was 40. The skin was blue, perspiring, and cold. The abdomen was markedly distended. He vomited "coffee grounds." Vomitus. The bowels had been moving about every hour, with bloody movements. He died in a few minutes.

Autopsy. The intestines were tense dark red, and the belly contained a large amount of bloody fluid. The omentum was adherent to the body walls and contained one hemorrhagic area. The transverse and descending colons were both negative. All mesenteric veins and transverse gastro-epiploic veins contained clotted blood, and the terminal portion of the mesenteric vein was a firm, organized thrombus.

11. Kratzseisen. White, ? sex ? age. Extirpation of the spleen was done January 19. May 20, patient was seized with sudden pain in the back, worse on the left. By May 28 patient had definite ascites. May 30, looked bad, and

again had severe cramping pain, no vomiting, no peristalsis, ascites worse. June 11, exitus. Patient vomited once, just before death. Clinically had had polycythemia vera.

Autopsy. The portal vein was small and studded with thrombi. The middle loops of the bowel were fully necrotic, showed hemorrhagic infarction of the mucosa and muscle, and the veins were thick walled and plugged with thrombi. The upper loops showed punctate focal necroses. The large bowel was intact.

12. Lommel (cited by Kratzseisen). White male aged 42 years. Patient had had intestinal colic and bloody stools 2 years before death. Polycythemia and splenic tumor were present. He died of "embolus of superior mesenteric vein" and infarction of the bowel.

13. Loeb (cited by Kratzseisen). White female, aged 61 years. Patient was operated upon for a strangulated ileus but was found to have thrombosis of the portal vein and ileocolic vein at post mortem.

14. Brie (cited by Kratzseisen). White male, aged 42 years. Illness had been diagnosed as acute yellow atrophy of the liver. Autopsy showed portal thrombosis and infarct of transverse colon, no ascites.

15. Smith, W. White female, aged 28 years, was operated upon for an interval appendix. After operation, the abdomen became distended, she vomited, and was extremely constipated. Temperature rose, the abdomen became silent, and obvious peritonitis set in.

Autopsy. Thrombus of "ileocolic vein," with gangrene of portion of the ileum.

16. Smith, W. White female, aged 32 years. Patient had had a hysterectomy and appendectomy 4 months before. The onset was acute, with nausea, vomiting, and paroxysmal pain continuously. Temperature was 97 degrees, pulse, 64, respiration, 30. The next day enemas yielded blood. Patient lay on her back or side, knees flexed, and she was in great pain. The abdomen was distended and tympanitic, with definite rigidity of the lower quadrants. White blood cells numbered 20,400, polymorphonuclears, 85 per cent, urine, 1 per cent indican. Temperature was 99.2 degrees, pulse, 76, respiration, 20. On the third day there was more tympany, less peristalsis, and the lower abdomen was rigid and tender. The cervix was movable and not tender. Enema brought pure blood. The pulse was 100. At operation the peritoneum was found to be dark and free blood was present. Fifteen inches of ileum was dark and lustreless and the mesentery was thick and edematous. The margins of the lesion were sharp. No bands or adhesions were noted. The vessels were thrombosed for an undetermined distance. The loop was withdrawn, excised, and the ends of the ileum were sutured to the abdomen. Anastomosis was done 4 weeks later, patient recovered.

17. Lang. White female, aged 60 years. Hysterectomy had been done 2 years before. Three months before she had had a fall followed by nagging pain in the back. She was treated by a chiropractor. At last visit, she told him she was constipated and he pommaded her abdomen severely. On the way home she developed severe pain and nausea. She went to bed, applied heat, vomited a laxative, and took an ineffectual enema. She became distended and faint and dizzy. She called a doctor who diagnosed acute small bowel obstruction. Patient refused operation until next afternoon, during which time she had constant vomiting, developed tenderness, distention, and a weak pulse. On admission she had marked leucocytosis. No blood was present in the stools. At operation, considerable serosanguineous fluid was found as well as a few adhesions of the omentum to the anterior belly wall. In the lower ileum, an area 8 inches long, dark purple sausage like in consistency, and covered with "bloody lymph" was noted. The

mesentery was swollen and edematous. The vessels were still and cord-like from the involved area to the root of the mesentery. A resection of 14 inches of the bowel with its mesentery and a lateral anastomosis and ileostomy at the higher level were done. Patient recovered and was well 7 months later. Pathologist's report: The specimen consisted of 14 inches of the bowel which was deeply congested with mucous reddish purple. When the bowel was opened, the mucosa and walls appeared to be deeply congested, of deep purple color, and section showed practically all vessels with evidence of thromboses.

8. Report at Vermingling mittledeutscher Chirurgen. White male, aged 67 years. Pneumonia. Patient presented palpable tumor as big as a child's head below the right costal margin. Under local anesthesia about 1 section of small intestine was resected. Multiple thrombi were found in the main branches of the superior mesenteric vein. Patient died after 4 hours.

10. Warszawa. White male, aged 60 years. The past and family history was essentially negative. Patient suddenly seized with generalized abdominal pain and vomiting. The vomiting was brown in color. The pain was chiefly in the middle, about 1 inch below the umbilicus and toward the left lower quadrant. The bowels were completely constipated. He took Epsom salts without relief. The abdomen was moderately rigid, marked tenderness was noted below the umbilicus and in the left lower quadrant. Peristalsis was visible. When blood cells numbered 27,000, polymorphonuclears, 98 per cent. At operation, extensive thromboses of jejunum and ileum were found, with considerable free fluid in the abdominal cavity. About 1 foot of bowel was involved. Resection with lateral anastomosis was done. Convalescence was stormy but patient finally recovered. Pathologist's report: The specimen was a piece of intestine 3 centimeters long, hemorrhagic, discolored, swollen, and very friable, with about 1 centimeter of mesentery. The lumen was filled with blood. Microscopically the wall was edematous, filled with extravasated blood and leucocytes. The mucosa was greatly swollen and hemorrhagic. The epithelium was destroyed. Some vessels were thrombosed, others clear. Sections through the mesentery showed some thromboses, and some veins with acute phlebitis. Diagnosis: acute phlebitis of the mesenteric veins, thromboses, hemorrhage in intestinal wall, no gangrene.

10. McClumbach. White male, aged 4 months. October 14, bowel movements were less than normal, stools clear. Next day child was apathetic, listless, and had no bowel movement. Caster oil and second course gave small amount of bright blood. He vomited that night. October 16, he was brought to the hospital, vomiting. The abdomen was slightly distended, with no palpable masses. Temperature was 101 degrees F. A large high fever returned clear. The temperature rose to 104 degrees overnight and symptoms became generally much worse. At operation small amount of dark red fluid was found. The distal ileum for 5 inches was firm, doughy, collapsed, and blue black in color. The mesentery appeared the same near the base. The belly was closed. Diagnosis: thromboses of mesentery. Patient died next day. No autopsy was performed.

Rabowitz. White female, aged 4 years. Periods had become irregular and profuse for last 3 months. September 16, she had severe abdominal cramps, localized in the epigastrium and radiating to the lumbar regions. After 24 hours pain was less severe but persistent sensation was present in the hypogastrium. Temperature was 99.6 degrees, pulse, 92 white blood cells, 2,400, polymorphonuclears, 70 per cent. The abdomen was enlarged and solid tumor mass about the size of 7 months' gestation was felt in the pelvis. Panhysterectomy was done on

September 21. She vomited next day. Temperature was 99.2 degrees, pulse, 96. The next day temperature and pulse were the same but vomiting was more frequent. October 1 the condition remained the same. The bowels moved with ease. No distention or distension was present. There was slight pain in the lower part of the abdomen. By October 3, pulse had increased to 114, vomiting was almost constant and with fecal odor but the abdomen was still soft and not tender. At operation, no free fluid was found in the abdominal cavity. In the left side of the cavity was noted a coil of small intestine about 9 inches long, purplish blue, distended to about twice normal size. The corresponding mesentery was edematous, hard, and distended. The abdomen was closed and the patient died in 4 hours.

12. South, W. White female, aged 28 years. As she had symptoms of chronic appendicitis, appendectomy was done. After operation patient vomited slightly the abdomen became distended, and complete constipation set in, temperature rose, and the patient died. Autopsy revealed thrombosis in the "ileocolic" vein and gangrene of part of the ileum.

13. Frank, L. White male, aged 8 years. Patient suffered a sudden onset of abdominal cramps in morning, rapidly became moribund, and died. Autopsy: Gangrene of entire cecum, terminal ileum, ascending colon, and transverse colon as far as visible. The small intestine and appendix were normal. There was large amount of bloody fluid in the abdominal cavity. A Meckel's diverticulum was present. Cause of death: peritonitis from mesenteric thrombosis.

14. Mason, J. M. White female, aged 35 years. She had had suspension, right subpergo-splenectomy and appendectomy some months before. She had feeling of fullness after meals. Patient was suddenly seized with pain, nausea, vomiting, distention. Operation revealed an adhesion from the stump of the right broad ligament to the outer surface of the mesentery. The intestine was dusky necrotic, and showed no sharp line of demarcation below though sharp above. Fifteen inches of ileum was removed. Recovery.

15. Parker. White female, aged 40 years. Patient complained of chronic constipation for 4 days. The condition had become bad 7 days before and the last movement had contained hard, lumpy lumps. On the afternoon of admission she was seized with severe pain in the left lower quadrant, later becoming generalized. The pain was sharp and distressing. She vomited three or four times. Patient was not in shock. She showed general abdominal tenderness and slight rigidity. Operation. A piece of bowel 9 inches long was removed along with piece of mesentery. Death occurred in 24 hours. At autopsy the abdomen was found to contain 500 cubic centimeters of bloody fluid. The bowel was discolored from anastomosis to within 12 inches of the ileocecal valve. Thromboses were found at junction of the splenic and superior mesenteric veins, extending almost to the spleen, into the portal vein, and down the superior mesenteric vein. The liver showed thrombosis at the portal radicles. Microscopic examination. The pancreatic vessels contained arteriovenous thrombi and part of the tissue degenerated the liver areas of degeneration, irregular in shape with some vessels thrombosed. Diagnosis: Thromboses of splenic mesenteric, and portal veins. Pressure by head of pancreas on junction of the splenic and mesenteric veins.

16. Wilson. White female, aged 25 years. Five days before the patient had been seized with pain which was colic like at first but later became continuous and severe. She vomited several times and felt better. Three days after onset, the pain became much worse and the vomiting more frequent. There had been no bowel movement for

days before admission, in spite of enemas. The abdomen was distended and slightly tender below and to the right of the umbilicus. An indefinite tumor mass was palpable in this region. Tympany and shifting dullness were present. Operation bloody fluid was found in the peritoneal cavity. The small bowel was blue and lustreless from "upper part" to within a few feet of the ileocecal valve. There was no sharp line of demarcation. The arteries were engorged and the veins blue and cyanotic. A collection of firm clots formed a mass in the upper portion of the mesentery. The abdomen was closed, it was felt that it would be too much to resect. The vessels looked as if the inferior mesenteric vein was taking over the function of the superior vein. Convalescence was uneventful.

27 Ross. White male, aged 46 years. Patient had had two attacks one 6 months and the other 1 year before. Two days before admission he had developed pain in the right lower quadrant, had had no bowel movements and the abdomen had become distended. A palpable mass was felt in the right lower quadrant. Operation was done 4 days after admission. The bowel around the cecum was gangrenous. There was no mechanical obstruction. Autopsy showed through the operative wound, thrombosis of veins from the ascending colon.

28 Ross. White male aged 52 years. Patient gave a 7 day history of pain, vomiting, and constipation. He had not been operated upon. Patient died 24 hours later. "Mesenteric thrombosis with gangrene of proximal 4 to 6 feet of ileum."

29 Laws. White male, aged 10 years. Patient had had acute abdominal pain followed by vomiting. A course of colamel was followed by passage of a large quantity of blood, a few hours later two small bloody stools. The severe colic like pains continued with vomiting. Four days later the abdomen was distended moderately, rigid, tender, especially below and to the right of the umbilicus. Feces revealed nothing but the presence of old blood. He was completely constipated and had complained for several years of abdominal pains in the mornings. White blood count was 17,600, polymorphonuclears 86 per cent. At operation, considerable bloody fluid was found in the abdominal cavity. Two feet of small intestine was found to be distended, edematous, and purple in color. The line of demarcation was sharp at both ends. A kink was found which was thought to be secondary to other pathological conditions. The mesentery was studded with hard lymph nodes of various sizes, thought to be tuberculous nodes. The mesenteric veins corresponding to the damaged segment were thrombosed. No resection was done. Patient was very ill for 2 more days and finally recovered. There was no return of the abdominal symptoms present before operation.

30 Nifong. White male, aged 26 years. The past history revealed a similar attack 4 months before, for 5 days. The present onset was sudden with vomiting. He was given castor oil, enemas, and morphine. Temperature was 97 degrees. The abdomen was rigid. Operation was done 16 hours later. A perforated appendix and "thrombosed mesentery in the lower part of the ileum" were found. The appendix was removed and 45 inches of ileum. Patient became worse, developed wound infection, distention, dark bowel protruding into the wound, and died 11 days after operation. Autopsy was not granted.

31 Nifong. White male, aged 21 years. Patient gave the usual story, with a 6 days' delay. Bloody fluid was found in the abdomen and all the intestines were discolored. Resection was done of 60 inches of the worst looking bowel and mesentery, which was "hard and thrombosed." Death occurred 5 hours after operation. No autopsy was granted.

32 Brady. Colored male, aged 51 years. Bilateral inguinal hernias had been operated upon and at apex of the right sac there was found a large abscess. The wall of the abscess was sutured to the abdominal wall through the right rectus incision. Patient died 4 days later. Autopsy thrombosis of inferior mesenteric vein, septic thrombosis of portal vein, no intestinal changes.

33 Brady. White male, aged 49 years. Patient had had three admissions for cirrhosis and diabetes. He developed sudden low abdominal pain 4 days before admission and died 2 days later. Autopsy thrombosis of portal and superior mesenteric veins, hemorrhagic infarction of intestine, diabetes, cirrhosis of liver.

34 Brady. White male, aged 52 years. Patient gave a history of 3 weeks of pains in the abdomen and occasional vomiting, 5 days of increased severity. Operation showed a gangrenous gut and engorged and blackened mesentery. The loop of the gut was brought out but was not resected. Enterostomy was done. Death occurred in 2 days. Necropsy thrombosis of mesenteric veins, necrosis, and gangrene of small intestine, general fibrinopurulent peritonitis.

35 Brady. White female, aged 45 years. Patient had been on medical service with Raynaud's phlebitis, and thrombosis of the left iliac vein. She had had 10 days of pain in the lower abdomen, and 1 day of vomiting. There was marked tenderness. At operation, a mass was disclosed in the upper abdomen made up of matted loops of bowel near the point of gangrene. Thirty inches of bowel was removed and a lateral anastomosis was done. The patient recovered.

36 Brady. White female, aged 31 years. Patient had had severe back pain and vomiting for 8 days. This was replaced by epigastric pain and delirium. Red blood cells, 7,680,000, hemoglobin, 112. At operation, a coil of intestine, distended and black, was noted. No pulsation was present in the mesenteric arteries. Resection of 60 inches of the bowel and lateral anastomosis were done but patient died in 24 hours. Autopsy polycythemia, atrophy of the liver, thrombosis of branches of portal vein with extension to mesenteric veins from stomach, intestine, and spleen, hypoplasia of bone marrow, infarction of small intestine and acute peritonitis.

37 Brady. White female, aged 24 years. Patient gave a history of rheumatic fever and edema of ankles. She had had a miscarriage 10 days before admission. She was suffering from sudden pain and vomiting. She was admitted to the hospital after having been in irrational state for 30 hours. The white blood count was 23,000, temperature, 102 degrees. Mitral stenosis and insufficiency, rigidity and spasm of the abdomen were noted. Operation consisted in the removal of 40 inches of gangrenous mesentery and intestine. The peritoneal cavity contained considerable bloody fluid. A secondary anastomosis was done and the patient recovered. Premortem thrombi and white cells were found in the vein lumina and walls.

38 Johnson. White male, aged 55 years. The past history was negative. The present illness was sudden, with general abdominal pain. Vomiting followed 30 minutes later, along with an increase in pain. Patient had had no bowel movement since the day before. There was a board like rigidity with marked tenderness. Temperature was 95.2 degrees, pulse, 52. There was discoloration of the abdomen as seen in an ectopic pregnancy. Operation disclosed bloody fluid in the abdomen. The mesentery, part of the jejunum, and part of the ileum, were of a dark purple color. "Mesentery was so thickened and intestine so edematous and so moist that the diagnosis was made of a thrombosis or embolism of the mesenteric veins rather than of the arteries." Four feet and 2 inches of bowel was resected and patient made an uneventful recovery.

39. Falkenberg. White, 7 age, 7 sex. Patient came to the clinic with symptoms of divert. Stools had been bloody. Operation showed thrombosis of the superior mesenteric vein. Its secondary gangrene of the bowel. Involved loops and corresponding mesentery were resected. Patient was discharged well.

40. Rose. White male, aged 45 years. Onset was sudden, with pain in the right lower quadrant, followed by vomiting. Purgatives gave no result. There was no fever or chills. He had had previous attacks, 6 months and soon before. The abdomen was distended with tumor like fulness in the right lower quadrant, and it showed marked tenderness and rigidity. Peristalsis was present in the upper and left lower quadrants. Rectal examination revealed marked tenderness. It was operated upon 4 days after admission to the hospital with diagnosis of appendicitis. The bowel as found to be gangrenous, and it ruptured during operation. It atrophy the veins leading to the ascending colon were found to be thrombosed.

41. Rose. White female, aged 37 years. She had had Culture suppurative operation about 30 days before. After week, she developed phlebitis of the left superficial vein with extension to the iliac vein. The abdomen became distended, tympanitic, and tender, and the patient developed pain, nausea, and vomiting. The bowels moved by enema and patient recovered. About further signs of obstruction. Bacillus coli was recovered from the blood stream.

42. Miller H. A. White female, aged 7 years. Onset as sudden. It was in the right upper-belly pain, chills, and fulness. She gave past history of "bilious attacks." By 12 she had tender rigid abdomen she had been coming since the previous evening. Temperature was 4 degrees, pulse, 80. At operation, serosanguineous fluid was found in the belly with 20 inches of gas gangrene bowel, reaching to within 4 inches of the cecum. In the center of diverticulum 3 inches long, adherent to loop of bowel. This had twisted and strangulated its blood supply setting up thrombosis, which extended into the higher mes. Resection was done with complete recovery of the patient.

43. Addison. White female, aged 41 years. Onset was sudden with continuous pain, followed by swelling of the abdomen. She vomited once. On admission to the hospital she was pale, in state of collapse and with prominent, tender swelling of the abdomen, like 6 months' pregnancy. There was no visible peristalsis, some lateral fulness. At operation, serosanguineous fluid was found in the abdomen. The intestine, in dark and discolored from within 3 inches of the cecum for distance of about 9 to 10 feet. There was an abrupt demarcation above and below. Resection and jejunocolostomy were done. Patient was discharged well.

44. Gibson. White female, aged 34 years. Onset was sudden with severe abdominal pain referred to the right of the umbilicus. The pain let up for a while but was followed by vomiting and complete bowel stasis. There was letup for 5 days. She was admitted to the hospital, at which time the temperature was 97 degrees, pulse, 80, respiration, 20. The abdomen was slightly distended and she frequently vomited fecal material. Peristalsis was not visible. Examen was about result. Operation revealed 10 inches of disintegrated small bowel with thickened mesentery deep chocolate in color. The mesentery was soft, adreous, and friable. The veins were thrombosed. Resection and lateral anastomosis was done with recovery.

45. Murray. White female, aged 14 1/2 years. The past history was negative. The present illness began with sudden attack of acute abdominal pain. Bowel movement had occurred earlier in the day. There was no vomiting. Temperature was normal, pulse, 140. The abdomen was tender with no distention. She was reoperated 3 hours

T three hours later she had a second attack, and 3 hours later she was in collapse. She was operated upon 30 hours after onset. Operation consisted entirely in drainage. Post-mortem, 6 hours later revealed no feet of small bowel distended and with early gangrene. At base of the mesentery was caecum lymph node from the region of which the thrombosis spread backward to both arteries and veins. The bowel had a sharp line of demarcation.

46. MacLeod. Male, 7 age. April 4, splenectomy had been done for pericardiac aneurysm. Two hours after operation there had been copious hemorrhage from the aneurysm, followed by second hemorrhage 6 hours later. Clotting time was delayed. Clotting in full dose was given for 4 days. May 4, he suffered severe abdominal pain with nausea, more in the lower right quadrant. The temperature and pulse were above normal. He had slight vomiting and diarrhea. May 30, abdomen was distended, free fluid was present in the abdominal cavity and mass was still palpable. Vomiting as not urgent or projectile in nature. Temperature and pulse were above normal. At operation, some coagulation of clot of small intestine, gangrenous as result of thrombosis in middle of the superior mesenteric vein, was noted. Resection was done of the gangrenous intestine and sufficient living intestine to be left outside the limits of the thrombosis. Death occurred in 4 days. Post-mortem revealed that the thrombosis extended into the mesenteric veins and up into the portal vein, the splenic vein was filled with recent clot thrombosis.

47. Brady. White female, aged 50 years. Patient was admitted to the hospital with aneurysm. Sordation and cardiac decompensation. She had a distended abdomen, but no pain. On the fifth day of the hospital she developed sudden severe pain and died in 24 hours. Post-mortem examination revealed arteriosclerosis, atherosclerosis, peritonitis, thrombosis of the superior mesenteric vein, and local orthogic infarction of the intestine.

48. Eliot. Female, aged 37 years. Patient had had 3 previous operations. She had varicose veins. A year and half ago she had falls striking her abdomen. After the fall she suffered occasional soreness in the lower abdomen. The onset of the present illness was sudden with acute colic, shooting pain from right to left then the navel. The pain moved down and. Two hours later she began to vomit. The bowels had moved few hours before the attack and afterward, with nausea. There was no gas or blood. Physical examination showed that the whole belly was tender, more so in the middle. There was symmetrical rigidity of both rectus muscles, no distention, there were sounds of active peristalsis. Rectal examination was negative. Several hours later, distention began and tender mass was felt below the navel both in front and rectally. At operation, bloody fluid was found and 3 feet from the ileocecal valve was loop of intestine 5 inches long, dark purple, and covered with fresh fibrin. There was sharp line of demarcation. The mesentery was infiltrated and the veins contained thrombi, while arteries did not pulsate. Resection and anastomosis were done and the patient recovered.

49. Eliot. Male, aged years. Several months before, patient had had similar attack, less severe, lasting 48 hours. Thirty four hours before he had had severe sharp pain around the umbilicus, increasing so intensely, not relieved by morphine. He vomited once. The bowels, originally constipated, moved several times, with catarrhs, no blood. The temperature was 99 degrees, pulse, 44, respiration, 36. The abdomen was slightly distended, aneurysmal, and tender principally in the right lower quadrant. Sounds of active peristalsis were heard. Rectal tenderness was in the left. Operation disclosed 4 inches of bowel, black in color 10 feet from the cecum. The mesentery was black and

swollen and without pulsation. The veins did not bleed. Patient recovered after abscess in the scrotum, fecal fistula, and right femoral phlebitis.

50 Eliot. Male, aged 60 years. Patient had had typhoid and phlebitis years before. Two days before admission to the hospital he had had abdominal discomfort and nausea. The next day his condition was about the same. He tried indigestion remedies but became worse, with pain settling in the right lower quadrant. The bowels began moving and he passed bismuth taken during the first day. There were tenderness and rigidity on the right in the region of the umbilicus, no distention. Pulse was 120, white blood cells, 25,000, polymorphonuclears, 95 per cent. At operation, 14 inches of purple colored bowel, 10 inches from the cecum, was resected. The veins were thrombosed and had no pulsation. Twenty-four hours later, patient was in good condition but developed sudden severe pain. The abdomen was reopened and a perforation was found 6 inches from the cecum. Death occurred 8 hours later. Microscopic examination extensive venous thrombosis.

51 Eliot. Male, aged 38 years. One hour after daily bowel movement, he was seized with general abdominal pain, dull, constant, and persistent, no nausea or vomiting. He was relieved by morphia that night. The second day, the same condition prevailed, with the addition of bloody stools. A high oil enema gave dark blood. On the third day, the pain was less, temperature, 100, pulse, 80. Patient looked well. There were tenderness and rigidity in the right lower quadrant. Rectal tenderness was bilateral. There was no palpable tumor. Operation disclosed bloody fluid, 2 feet from the cecum, 20 inches of necrotic bowel with sharp demarcation. The veins were thrombosed and had no pulsation. Resection of 32 inches of bowel, anastomosis, recovery.

52 Weil (cited by Eliot). Female, aged 52 years. Obstipation had been noted for 3 years. Present illness began with sudden abdominal pain, general, and vomiting. Belly was soft with tenderness and resistance over the bladder and the left lower quadrant. There was slight distention. Pelvic examination showed sensitive elongate tumor. Pulse was 90, temperature, 97.6 degrees. Operation disclosed bloody fluid in the abdomen, 2 feet of bluish red intestine with sharp line of demarcation, mesentery edematous, and veins thrombosed. Resection and ileocolostomy resulted in recovery.

53 Davis (cited by Eliot). White female, 45 years of age. Five years before, patient had a similar attack for 2 or 3 days and again 2 years before, both of which cleared up. "For days" she had had general mild abdominal pain. Patient menstruated and pain became worse and paroxysmal in type. The pulse and temperature were subnormal. Patient was in mild shock but operation was delayed. The next day she vomited and had tenderness and slight rigidity. Enema brought bloody fluid. The abdomen was distended, fluid was felt in the flanks and peristalsis was visible. Operation was done about 40 hours after onset. Bloody fluid was found in the abdomen. There were 18 inches of small bowel, rigid and deep purple in color. There was a sharp margin above and below. The mesentery was thickened and the vessel thrombosed. Resection was done with secondary anastomosis. Patient was discharged well.

54 Mole. ? race, male, aged 42 years. Patient was admitted to the hospital during a cholera epidemic. Onset was 24 hours before, with vomiting, watery diarrhea, and cramps in the legs. He was pulseless and lived only 24 hours. The abdomen became distended shortly before death. Autopsy showed the lower part of the small bowel distended, 3 feet at lower end dark chocolate color, with here and there thin exudate on the surface, most of the

peritoneum was shiny, mesenteric lymph nodes were enlarged. Some mesenteric veins were thrombosed from the foot of the mesentery to the bowel wall, others were free. The bowel contents were bloody rather than rice water in appearance. Microscopically the mucosa was markedly thickened and filled with congested blood vessels and hemorrhages. Many foci of necrosis were noted in the mucosa and wall. Peyer's patches were markedly congested.

55 West. White female, aged 20 years. Patient was admitted to the hospital giving a history of severe abdominal pain for 3 days, increasing in severity and associated with vomiting. The abdomen was distended and tender, and patient was unable to co-operate. On deep forcible palpation, a mass was felt to the left of the spinal column. Pulse was 120, temperature 101.5 degrees. Operation was done 8 hours later. All of the small intestine appeared far advanced toward gangrene. The superior mesenteric vessels were constricted by a band passing across the abdominal cavity just above the umbilicus, which proved to be the mesentery of the cecum which had revolved toward the left. The appendix was inflamed. The adhesions were freed, the appendix was removed, and the cecum revolved and fixed. The bowel began to regain color and was not resected. Patient recovered. Double pyosalpinx was not operated upon.

56 Michael. White female, aged "young". Young woman had previously been well except for a miscarriage 4 months before. For 1 month she had had occasional vomiting and suddenly developed intense, paroxysmal umbilical pain. The spleen was enlarged, and the patient showed an anemia of 38 per cent. At operation 3 meters of the small bowel, edematous and discolored along with the corresponding mesentery were noted and resected. The veins were found to be thrombosed. She recovered. One month after operation she developed femoral phlebitis which soon subsided.

57 Geppert. White male, aged 40 years. Three days before he had had a sudden attack of severe colic-like pain in the upper abdomen, no fever, diarrhea, obstipation, or vomiting. The last bowel movement was 30 hours before admission on the third day. There was some tenderness in the left upper quadrant, with slight rigidity. No free fluid or peritonitis was found. After a short time patient had an exacerbation of symptoms, vomited bloody fluid, went into collapse, and died. The condition was diagnosed clinically as mesenteric thrombosis. Autopsy revealed 500 cubic centimeters of serosanguinous fluid in the lesser peritoneal cavity. From the beginning of the jejunum for 1 meter, the bowel was dark blue red in color and the mesentery thickened toward the portal region. The mesenteric vessel contained thrombus with dark center and pale margin. The jejunal stem of the superior mesenteric vein was occluded throughout by dark red, fresh thrombus. The wall of the vein was three times normal thickness as was true of the splenic and portal veins. The oldest thrombus 6 centimeters long was found near the splenic portal junction. The last 4 centimeters of the portal stem was clear. The stomach mucosa was hemorrhagic and doughy. Microscopic examination confirmed the gross. The intima of the veins was thickened and the elastica markedly increased. Many infarcts were found in the liver and were thought to represent old and recent phlebitis. Fat necrosis was found in the pancreas.

58 Bucura. White female, aged 23 years. Patient had had a normal delivery on January 6, after a pregnancy which gave symptoms of impending eclampsia but never progressed to actual convulsions. On January 16, she was suddenly seized with vomiting and cramps. She became completely constipated. The next day she was much worse and the abdomen was generally tender. At operation the

intestines were found to be gangrenous for 10 centimeters. During operation, the process could be seen extending and the patient died 30 hours later. The necrosis of the resected bowel was intact, but the wall was gangrenous and the veins were thrombosed.

59 Miller L. I. White female, aged 3 years. While skating, the girl fell and was locked in the abdomen. She had dull pain in the right lower quadrant for 3 days and then was seized with sudden severe, generalized pain. She came to the hospital 4 days later after being seen by four doctors. White blood count was 35,000. She died very shortly from shock. Autopsy revealed thromboses of the veins of the descending colon and involvement of 3 centimeters of bowel.

60 Peyrot White male, aged 3 years. Patient was seized with sudden, violent abdominal cramps and fecal vomiting. This lasted about 24 hours before operation. Three and one-half meters of small intestine were found to be gangrenous. Cecostomy was done and the infected bowel was returned to the abdomen. Patient died 4 hours later. Autopsy confirmed the clinical diagnosis of thrombophlebitis of the mesentery with another occlusion and infection. Five and two tenths meters were found to be involved, starting 30 centimeters from the ligament of Treitz.

61 Skel White female, aged 3 years. Seven weeks postpartum, patient had bad phlebitis. She got up and walked around and was seized with severe abdominal pain followed by vomiting. She died in 22 hours without operation.

62 Bunker White male, aged 47 years. Illness began as malaise (short pain). Pain developed about 6 hours later along with vomiting, distention, and shock, but without bloody or fecal vomiting. Operation consisted in resection of 433 centimeters of small intestine which was gangrenous. A slight amount of putrid feces was found. Microscopic examination showed marked arteritis and thrombosis of both veins and arteries. Patient recovered.

63 De Quibus and Antelope White male, aged 35 years. For 3 days patient had had bilious vomiting, retention of gas, and meteorism. Diagnosis: pseudotumor. At operation, fecal, aerogramenous fluid was found in the abdomen. In the duodenum, loop of bowel 5 centimeters from the duodenal valve, 5 centimeters long which was black and dilated, was noted. Twenty centimeters was resected. Grossly the mesenteric veins were thrombosed. Patient recovered.

64 Morand White female, aged about 30 years. Because patient could not speak French, very little history was obtained, but apparently she had had cramps and vomiting for 4 days. The abdomen was distended and tympanic, vesicles were black, and stools were tarry. Autopsy revealed large quantity of aerogramenous fluid. The epiploons were retracted and blood soaked. Two meters from the duodenum, the bowel was distended and was red in color. The lumen was sharply dilated. The mesentery was infiltrated with blood for about 20 centimeters. The lumen of the bowel was filled with aerogramenous fluid. Dissection of the vessels showed the arteries to be free and the veins thrombosed as far as, and into, the portal vein. The liver was catarrhal, the gall bladder chronic. Microscopic examination revealed the liver sinusoids thrombosed and the nodules peeled off. The arteries showed endarteritis obliterans. The mesenteric vessels contained partially organized thrombus and thick media with separation of muscle fibers. The air ascension occasionally were thrombosed.

65 Desplais White male, aged 1 year. Patient had had attacks of dysenteric character, of hemorrhagic dysentery of pain and hemorrhage of appendicitis, and of typhlo-

appendicitis crises in 9 7 1914, 1915, 1916, 1917. In April, 1915, he had had severe pain medial to McBurney's point. On May 5, he had had black, bloody diarrhea. On May 7 he passed "saucer" of black blood and developed some fever. On May 10, he developed alboria purpur hemorrhagica. On May 14, he had severe attack of colic, bloody diarrhea, had sensation of impending death, and showed profound alteration in condition. The belly was ballooned, with tenderness and spasm about the umbilicus and in the right lower quadrant. Rectal examination revealed tenderness. At operation, bloody fluid was found in the belly. Twenty centimeters from the cecum, the ileus was gangrenous and the corresponding mesentery was edematous and blood soaked. Sixty centimeters was resected and the patient finally recovered after stormy course. Histological examination revealed massive degeneration of the mucosa, submucosa, polymorphonuclear leukocytic infiltration with fragmentation of the muscle fibers, serosa elevated by liquid exudate, adjacent zones of edema of mucosa and musculature, thrombophlebitis of the terminal branches of the superior mesenteric veins.

66 Mathis and Ahlstrom White female, aged 14 years. Patient had had 3 days of pain in the abdomen and abundant fecal vomiting. The pulse was weak, the abdomen distended and tender. The temperature was normal. After 8 days of sickness, the symptoms ceased only to recur in another 6 days. This time she was constipated and had fever as well as fecal vomiting. Autopsy revealed the entire ileum retracted. The mesentery showed extensive thrombosis and the arteries free. No cause for the condition was determined.

67 Hartglass White female, aged 31 years. Patient gave the usual history of sudden onset, pain, vomiting, and distention. An infarcted mesentery was found. Operation, with some unknown, but the bowel had apparently recovered. The abdomen was closed and the patient recovered.

68 Rasmussen White male, aged 77 years. Patient had always been healthy until 4 months before admission. He developed mild cramping pain which disappeared periodically, but gave history of bloody stools. The abdomen was found to be tense and tender, especially in the right lower quadrant, about the level of the umbilicus, with sensation of pain or tenderness. Temperature was 101.5, green pulse, 60. The tongue was coated and dry. Patient developed constipation and retention of gas. A tentative diagnosis was made of bowel tumor or appendicitis. Enemas and rectal tube for 3 days gave little gas. For 3 days more he was given castor oil, had bowel movement and felt better. Temperature became normal, "tumor" disappeared. Eight days later he became worse, had distention, tenderness, and appeared very ill. At operation, cloudy exudate was found. The appendix was coated with fibrin. A sausage like tumor was present in the right upper quadrant under the liver and was found to be made up of loops of small bowel which measured 75 centimeters in length. No anastomotic obstruction was found. The mesentery was markedly swollen, edematous, and friable. The vessels were found to be occluded. The liver was nodular and small. One meter was resected. Patient died after 31 days. A topey disclosed thrombosis of the portal and mesenteric veins, hepatic cirrhosis, hemorrhagic infarct of some remaining bowel.

69 Rasmussen White male, aged 5 years, had previously been well. He had been an excessive drinker and smoker all his life. Four days before he developed malaise, mild epigastric pain, and vomiting. The pain shifted to the right lower quadrant, he had no fever, but pain increased moderately. The family doctor said that there was tenderness over McBurney's point and perforation of the appen-

dix was thought of. Physical examination revealed distention, spasm, and tenderness in the right lower quadrant, less on the left. Temperature was 37.1 degrees C, pulse, 104. He had passed gas and vomited the day before. Operation disclosed cloudy fluid in the abdomen and "secondary appendicitis." A tumor was felt which proved to be small bowel and was gangrenous. No kinking or mechanical obstruction was present. The mesentery was swollen and gray in color. Resection of 16 meters was done. The veins of the mesentery were found to be thrombosed. Autopsy next day revealed the portal vein stem thrombosed from a narrow point behind the pancreas down into the mesenteric vein but clear above this point, cirrhosis of mild degree, old thickening of the vein wall at the initial point of the thrombosis which was thought to represent an old canalized thrombus with new thrombosis superimposed. Infarction of the bowel had extended.

70 Hedlund. White female, aged 36 years. Patient had a thrombosis in the superior mesenteric vein and ileus. Nine and a half months previously she had had a tubal abortion with operation. Since then she had had occasional colic like pain. On November 28, 1913, she was seized with severe pain in the entire abdomen, diffuse. Temperature was 37.4 degrees C, pulse, 74. After several hours, the pain became less. There were occasional peristaltic sounds over the umbilicus, no distention, pelvis negative, no abdominal resistance, no flatus. At operation a resection of 4 centimeters of jejunum was done along with the adjoining mesentery. Patient died during the night. Autopsy revealed hemorrhagic infarct of intestine at site of operation and mesenteric venous thrombosis.

71 Bonnet. White female, aged 28 years. Patient was operated upon on December 20 for pelvic inflammatory disease. On August 30 of the following year she developed sudden epigastric pain, not relieved by morphine, and vomiting, not fecal. She was given castor oil, enemas, pituitrin, and olive oil per rectum, without results except some flatus. No blood or distention was found but there was slight rigidity of the muscles. She became worse. Pain became rhythmic, and masses became palpable in the abdomen. Operation revealed bloody fluid in the abdomen. The bowel was infarcted as well as a V shaped piece of mesentery within 2 feet of the cecum. A resection of 224 centimeters of ileum was done and as well an end to end anastomosis. Patient was in shock but recovered and left the hospital. She was well 6 months later.

72 Silbol and Bourde. White male, aged 60 years. Patient was admitted to the hospital, vomiting, with distention, and without passage of gas. He gave history of sudden onset of pain in the left flank which became worse. A palpable mass was noted in the left iliac fossa—diagnosed carcinoma of the sigmoid or volvulus of the pelvic colon. At operation a loop of ileum, 25 centimeters long, was found, turgid and purple, in the iliac fossa. The mesentery was also involved. Resection and end to end anastomosis were done. Patient died 8 hours later. Pathological report the specimen consists of 32 centimeters of resected bowel with sudden transition between normal and infarcted bowel. Confirmed venous thrombosis microscopically.

73 Cabot Case 13502. White female, aged 46 years. Patient gave a history of trouble with abdominal discomfort, nausea and dizziness for many years more marked during last 5 years. Three years before she had had "intestinal gripe" at which time she passed large quantities of mucus. Seven weeks before she developed soreness in the epigastrium which became worse and moved to the left lower quadrant about 1 week before admission. No respiratory symptoms or jaundice were noted. The family history was positive for carcinoma. The past history was negative except for slight hypertension and subjective

symptoms. Patient walked into the ward but later was seen holding the abdomen as if in great pain. Examination was difficult because of obesity, but apparently she had a large tender liver, a movable tender mass in the left lower quadrant. Blood pressure was 140/70, white blood count 10-20000. The urine showed trace of sugar, slight trace of albumin, 15 to 20 white blood cells, and an occasional red blood cell at one examination. The stools and vomitus were guaiac positive, no free hydrochloric acid was noted. X-ray examination was negative. Temperature was 100.2 degrees, respiration, 20, pulse, 77, rising to 99. Four days later note states that patient was too ill for a barium enema. Constant vomiting and abdominal pain required morphine. July 1, 6 days after admission to the hospital, she was operated upon. The abdomen was found to contain much fluid. Thrombosis of the superior mesenteric vein branches, with gangrene of the intestines was noted, also thickening of the mesentery of the transverse colon. The bowel was resected and lateral anastomosis was done. Patient died the next day. Pathological report showed carcinoma of the stomach with two ulcer craters. Attached to the stomach carcinoma was a large tumor of the mesentery and transverse colon which, by pressure and direct growth around the vessels, caused thrombosis of both veins and arteries.

#### SUMMARY

Two new cases of intestinal obstruction caused by thrombosis of the mesenteric veins are presented along with 73 other cases collected from the literature and a general review of the literature from 1913 to 1933.

The pathological process is analyzed and an explanation given of the development of obstruction and hemorrhagic infarction following either arterial or venous occlusion.

A list of some of the more common etiological factors and predisposing causes is presented, with the conclusion that septic abdominal processes and cirrhosis of the liver are of the greatest importance.

A statistical analysis of several series of cases reveals the general incidence of the disease to be from 0.003 per cent to 0.007 per cent, and also that there has been a great improvement in the last few years, both in diagnosis and the results of treatment.

No definite symptom complex can be discovered to set the disease apart as a clinical entity, but rather it is classed as a fairly characteristic type of intestinal obstruction with diagnostic possibilities of about 60 per cent.

Treatment is limited to exploration and resection of infarcted bowel and mesentery, with a good prognosis in the cases operated upon during the first 12 hours of acute symptoms and an extremely bad prognosis after 48 hours.

#### BIBLIOGRAPHY

1. Addison, O. I. A case of thrombosis of a considerable portion of the superior mesenteric vessels without any discoverable cause. *Brit J Surg* 1917 5: 1-11.



- B VICK, A. U. cas d'obstruction des vaisseaux mésentériques avec résection de 4 mètres 35 cm. d'intestin grêle. *Lyon chir.* 1932, 63.
- BLANCHARD, J. H. Mesenteric thrombosis and embolism report of 35 cases. *South M J.* 9 6 9 8.
- BRADY LEO. Mesenteric vascular occlusion. *Arch Surg.* 1925, 65.
- BRIT. Quoted by Katschenko.
- BUTLER. Peritonitis. Mesenteric infarction. *Arch f Gynaec.* 1923, 9 275.
- BORVOY. Embolism. Mesenteric thrombosis with 87 inches of intestine resected. *Med Rec.* 1928, 93 302.
- CABOT CASE. 3502. *Boston M & S J.* 1927, 97.
- CHILDS, W. Ueber beschränkte Darmkranke. *Chirid. Ann.* 9 3 37.
- COTTE. J. Anat. & Physiol. London, 1866, 3 45. Quoted by Jackson, Porter, and Quinby.
- CORNETT, A. J. Mesenteric Vascular Occlusion. *Wm Wood & Co.* 1926.
- COTTON, H. R. Thrombosis and embolism. *New York M J.* 9 2 1374.
- DAVIS. Quoted by Ebbot and Jamison.
- DEWEY, J. B. Acute intestinal obstruction. Read before the New York State Medical Association Meeting, June, 1929. *New York State J Med.* 1929, 33.
- DEWEY, H. Note sur deux observations de thrombose mésentérique. *Arch d mal de l'appareil digest.* 1927, 7 670.
- EISENHART, A. A. and SCHULZ, H. A. Mesenteric vascular occlusion. *Surg Gynec & Obst.* 1913, 17 66.
- ELIOT F. J. and JACKSON J. W. Mesenteric thrombosis. *Ann Surg.* 9 3 63 313.
- FALKENBERG, Hs. Verfall report at Aerztlicher Verein zu Hamburg, Sitzung vom December 9 7. *Berl klin Wochenschr.* 9 4, 55 64.
- FLETCHER, C. W. Intestinal obstruction. *Texas State J Med.* 1924, 10 274.
- FRAZ, L. LOOM. Mesenteric vascular occlusion report of three cases in children. *Am J Surg.* 1913, 37 204.
- GILBERT, F. and SCHROEDER, K. Mesenterialvenen thrombose bei einer malign. entzündenden Phlebosklerose der Pfortader. *Berl klin Wochenschr.* 9 4, 5 30.
- GERMARDY. Falsche der Arterien mésentériques. *Wochenschr. Zisch.* 1924, 4 4.
- GROSS, S. C. Case of intestinal obstruction by thrombosis of mesenteric veins. *Lancet.* 9 7 224.
- GROSS, V. M. Intestinal obstruction. *Southwest Med.* 1925, 9 90.
- GROSS, Zentralbl. f. Path. path. Anat. 9 5, 10 13. Quoted by Jacobs.
- GUTHRIE, P. (de Békery). Étranglement rétrograde. *Revue de la thrombose des vaisseaux mésentériques dans certaines gangrènes intestinales.* *Bull et mémo Soc nat de Chir.* 1913, 50 74.
- HARTMANN, M. Intestinal intussusception. *Bull et mémo Soc nat de Chir.* 1913, 50 5.
- HEDER, W. J. Thrombosis and embolism of mesenteric vessels. *Hygien.* 9 7 1875.
- JACOBI. A. Polycythæmia and Mesenteric thrombosis. three observations on 2 adult females. *Ann. d. Gynæcol. & Med.* Chir. 1914, 4 555.
- JACKSON, PORTER, and QUINBY. Mesenteric embolism and thrombosis. *J Am M Ass.* 1904, 4 1499.
- JACKSON, C. M. Mesenteric thrombosis report of case with recovery. *Illinois M J.* 19 1 41 402.
- KARSTEN. Schwann. Corbl., 1897 vol. 15. Quoted by Jackson, Porter and Quinby.
- KATZ, EUGENE. Embolism and thrombosis of the superior mesenteric artery. *Surg Gynec. & Obst.* 1923, 33 385.
- KATZ, EUGENE. A. Polycythæmia and Mesenteric thrombosis. aus dem Pathologischen Institut des Kaiserlichen Stadtkrankenhaus. *Arch f path Anat.* 1921, 244 457.
- KATZ, EUGENE. Verfall report at Vereinigung mittelständischer Chirurgen. *Zentralbl. f. Chir.* 1923, 3 17.
- KOHN. Zur Diagnose der Embolie der Arterien mésentériques. *Wochenschr. Zisch.* 1924, 3 270.
- LARSON, L. M. Mesenteric vascular occlusion. *Surg Gynec. & Obst.* 1923, 55 54.
- LAW, G. M. Mesenteric thrombosis. *Ann Surg.* 1916, 63 370.
- LITTELL, M. Ueber die Folgen des Verschlusses der Arterien mésentériques superiores. *Arch f path Anat.* 1873, 63 180.
- LOOM. Ueber circumscribte gutturoseartige Endarteritis. *Deutsche med Wochenschr.* 1890, 3 45.
- LOOM. Quoted by Katschenko.
- LOOM, R. C. Mesenteric vascular occlusion. *J Am M Ass.* 1923, 17 309.
- McCLANAHAN, D. J. Mesenteric thrombosis, report of case four months of age; fatal. *Illinois M J.* 1924, 40 54.
- MASON, J. M. Thrombosis of superior mesenteric vessels, with successful resection of 65 inches of infarcted ileum. *Surg Clin N America.* 1922, October 337.
- MASON, J. M. Occlusion of mesenteric vessels. *Texas State Surg.* Ann. 1921, 24 113.
- MACLEOD, J. A. Acute intestinal obstruction. *Med Rev of Rev.* 1920, 26 30.
- McLEOD, J. A. Acute intestinal obstruction. *Am J Surg.* 1923, 19 153.
- MAISON, ALBERT, and AUSTIN, L. S. Fals. Cliniques. Étude de diagnostic dans un cas de thrombose des vaisseaux mésentériques. *Arch d mal de l'appareil digest.* 14, 8 64.
- McMAHER, P. R. Thrombosis in mesenteric vein. *Nederl Tijdschr. Geneesk.* 1925, 59 14. Abstracted in *J Am M Ass.* 1925, 85.
- MILLER, H. A. Thrombosis of the mesentery with report of case. *Southwest Med.* 1918, 5 1.
- MILLER, L. E. Mesenteric thrombosis, with resection of the intestine. *Colorado Med.* 9 9 16 43.
- MINTHILL, J. F. Mesenteric thrombosis. *Texas State Surg.* Ann. 1923, 3 3.
- MINTHILL, J. F. A case of mesenteric thrombosis on young organism from causative tuberculous gland. *Brit J Child Dis.* 9 4, 209.
- MORSE, R. How to Unusual pathological conditions of the intestine. *China M J.* 1920, 34 3.
- MORSE, PIERRE. Thrombose de la veine mésentérique supérieure. *Bull et mémo Soc anat de Par.* 1924, 94 44.
- MORSE, F. G. Some observations on mesenteric occlusion. *Am J Surg.* 9 3 29 185.
- OSWALD, W. Ueber Thrombosis im Gebiet der Veine mésentérique superior bei einem 14 jährigen Kalkendener. *Zentralbl. f. Chir.* 1920, 57 100.
- OSWALD, W. Ueber. Statistical survey of three thousand autopsies. *Standard Univ Press.* 1926.

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- 60 PEYROT, J Une observation de thrombophlébite  
mésaraïque primitive J de méd de Bordeaux,  
1920 41 355
- 61 ALTEFAGE Thrombose des vaisseaux mésentériques  
au niveau d'une anse grêle, réaction de l'anse,  
guérison Bull et mém Soc de chir de Par, 1918,  
44 904
- 62 PARKER, C B Mesenteric thrombosis, with report of  
two cases Canadian M Ass J, 1922, 12 655
- 63 RABINOVITZ, M Mesenteric venous thrombosis follow-  
ing an abdominal hysterectomy for fibroids New  
York M J, 1917, 106 71
- 64 REICH, A Embolie und Thrombose der Mesenterialge-  
fässe Ergebn d Chir u Orthop, 1913, 7 515
- 65 RONEY, W H Thrombosis in abdominal viscera M  
Clin N Amer, 1933, 16 845
- 66 ROSS, G G Mesenteric thrombosis Inn Surg,  
1920, 72 121
- 67 RUSZYNSKI, F Thrombose der Pfortader und der  
Mesenterialvenen als Appendicitisches Krankheits-  
bild Deutsche Ztschr f Chir, 1933 234 644
- 68 SILHOL and BOURDE Thrombophlébite mésentérique  
localisée Arch franco belges de chir, 1924, 27  
1016
- 69 SKEEL, D W Mesenteric thrombosis South Calif  
Pract., 1916, 31 125
- 70 SMITH, J F Mesenteric embolism and thrombosis  
Wisconsin M J, 1919, 18 1
- 71 SMITH, WILBUR Superior mesenteric thrombosis  
Calif & West Med, 1930 32 308
- 72 Idem Superior mesenteric thrombosis Southwest  
Med, 1928 12 549
- 73 TROTTER, L B C Embolism and thrombo is of the  
mesenteric vessels Cambridge University Press  
1913 Quoted by Larson and Collins
- 74 VIRCHOW, R Ueber die akute Entzündung der Ar-  
terien Arch f path Anat., 1847 1 272
- 75 WARSHTUTS, F C Acute mesenteric thrombosis, re-  
section, recovery A case report Am J Surg,  
1926, 1 281
- 76 WEIL Quoted by Eliot and Jameson, q 1
- 77 WELCH and MALL Quoted by Jackson, Porter and  
Quinby
- 78 WEST, J A Obstruction of the superior mesenteric  
vessels from bands with threatened gangrene of the  
greater part of the small intestine. Recovery Am  
J Obst & Gynec, 1921, 50 516
- 79 WILSON, K J G Thrombosis of the superior mesen-  
teric vein M J Australia, 1923, 2 386
- 80 WINTERS, W W and ANDERSON, W S Thrombosis  
of superior mesenteric vein Med Bull Vet  
Admin, 1932 8 311
- 81 WULSTEN, JOACHIM Heilung einer Thrombose der  
Vena mesenterica superior durch Resektion des ge-  
samten Duendarmes Zentralbl f Chir 1929,  
56 3155

## EDITORIALS

### SURGERY GYNECOLOGY AND OBSTETRICS

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JULY 1935

### THE SO CALLED LIVER DEATH SYNDROME IN SURGERY

CHARLES GORDON HEYD was the first to point out the significance of the so called liver deaths which sometimes follow biliary surgery and which are not to be explained by the usual factors of shock, hemorrhage embolism infection and respiratory complications. Such cases it is now recognized, fall into two distinct groups. In the first death occurs promptly after operation hyperpyrexia is the outstanding symptom and degenerative changes in the liver are the only notable autopsy finding. In the second group death is deferred for 10 to 14 days, or even longer uræmic symptoms predominate, and autopsy reveals the liver changes just described plus similar degenerative changes in the convoluted tubules of the kidneys. For these cases no universally applicable explanation has yet been advanced.

As the interest in this type of death has increased there has been an increasing feeling that the syndrome is not confined to biliary surgery but occurs and not infrequently in other postoperative conditions. Heyd in his

original communication mentioned that it might occur in both pancreatic and gastrointestinal surgery. Furtwaengler, Stanton, and Helwig and Orr observed it in cases of liver trauma, and the last named authors also noted it as a late complication of mammary carcinoma. LeVoe noted it after surgery for gastric ulcer and Connell who in 1931 had stated that the syndrome was never apparent except after biliary surgery withdrew the observation in 1934 and stated that he had since identified it after operations for ovarian cyst, uterine fibroids, interval appendicitis and ventral hernia. Heuer who has never seen it after biliary surgery observed it after a splenectomy for supposed Banti's disease. The 36 cases of postoperative heat stroke collected by Cutting only a few of which followed biliary surgery seem likely in the light of our present knowledge to fall into the same category.

In a study of the records of the New Orleans Charity Hospital for the last 7½ years, we have been able to locate 23 liver deaths after gall-bladder surgery this being the largest single group reported in the literature to date, as well as 5 cases of pancreatitis and 6 cases of liver trauma which clearly fit Heyd's original classification. Furthermore, in a series of casually selected recent autopsies comprising burns, intestinal obstruction, and thyroid disease we were able to find case after case in which there was evident a striking parallelism with the deaths which occurred after surgery for biliary and pancreatic disease and after liver trauma. In most instances, when the dis-

ical course was typical the postmortem findings were also typical, i e , necrotic changes in the liver, with or without similar changes in the convoluted tubules of the kidneys, depending upon how long the patient lived after operation had been performed or after injury had been sustained

Our own hypothesis which is based upon a study of the cases just listed and upon a series of personal experiments,<sup>1</sup> is that the same syndrome is apparent and the same underlying factors are operative in all of these conditions, as well as in many others, perhaps, in which it has not yet been recognized. In such cases, we postulate, the underlying factor is some degree of liver damage which is not incompatible with the strain of normal life but which is incompatible with the added

strain of disease or of trauma. When this strain is superimposed upon the existing hepatic disability, the damaged liver cells, failing in their function, release into the circulation some potent toxic substance. This substance, circulating in the blood, is excreted by the kidneys through the convoluted tubules, which, unfitted by nature for such a load, break under it. It seems not unreasonable to assume, further, that the liver kidney syndrome is a single pathological process, rapid hyperpyrexia deaths, in which only liver changes are apparent at autopsy, being simply the first stage of the process which, if it continues, later terminates in the uremic type of death, with renal as well as hepatic changes apparent at autopsy.

FREDERICK FITZHERBERT BOYCE

# EARLY AMERICAN MEDICAL SCHOOLS

## THE COLLEGE OF MEDICINE OF THE OHIO STATE UNIVERSITY

JONATHAN FORMAN B.A. M.D. COLUMBUS, OHIO

*Formerly Assistant Professor of Pathology, Lecturer on Diseases Due to Alchemy, The Ohio State University*

**I**n 1706 the Connecticut Land Company bought three million acres of land in the Connecticut Western Reserve and became the dominant influence in northeastern Ohio sending out a great many settlers from New England.

On March 3, 1834 the Ohio Legislature passed two bills of great significance: the Ohio State University which was destined to be established in Columbus by the same legislative body forty-two years later; the first was a charter for the city of Columbus which since its founding in 1786 had been a borough; the second was a charter for the Willoughby University of Lake Erie to be located at Chagrin, Ohio. This charter gave the power to grant degrees in the Arts, Sciences and Professions. Chagrin, later to be renamed in honor of its University Willoughby was at that time "a beautiful port to the northeasternmost corner of Cuyahoga County—distance 20 miles southeast of Cleveland. The village had the advantages of a library, lecture room, a historical society and a debating society where political, social and scientific questions were discussed. About 1830, the era of railroads had begun to intrigue the public mind. One of the various railroad projects which promptly rose in Ohio was to have a terminus at the mouth of the Chagrin River. The villagers had visions of Chagrin becoming a great lake port. With these expectations came the yearning for a great university.

As a result eleven citizens of the town for physicians and seven laymen, were created a corporation

under the name of Willoughby University of Lake Erie. Only the Medical Department, however, was organized. There were at least four reasons for this. In the first place there were several academies in the Western Reserve and graduation from any of these was considered in those days a great intellectual achievement and ample preparation for his unless perhaps one were to enter one of the professional Western Reserve Colleges nearby at Hiram, Ohio, was already a flourishing institution eight years old—while the year before to the westward at no great distance the Oberlin Collegiate Institute had opened its doors auspiciously so that there really was no great demand for an Arts College. In the second place, to the eastward there was no medical school nearer than the Fairbairn Medical College in eastern New York—four hundred miles away. In Ohio, the only regular medical school was the fifteen year old Medical College of Ohio at Cincinnati, nearly three hundred miles distant. In addition, the irregular Reformed Botanic Medical School at Worthington was 10 years old. It is also to be remembered that there was no medical school in any of the states west of Ohio. Therefore it appeared to these enterprising citizens that there was room for a medical school in rapidly growing northern Ohio, for all these pioneer communities were more in need of physicians than for any other professional group. In the third place, there was the splendid figure and personality of Dr. Wetzel Willoughby, the founder of the Fairbairn Medical School. He was interested in the town of



*Drawn by Henry Bacon in 1844*

Fig. The Willoughby Medical School at Willoughby.

Chagrin financially and in the project of the school. To the school, he made liberal donations. It was only natural that his advice should direct the university at once to medical education. Finally, in those days medicine was the cheapest form of higher education to promote and operate.

While the four local physicians on the board of trustees naturally found themselves on the original faculty along with certain others including Storm Rosa of Painesville, who was later to become "The Stormy Petrel of Homeopathy," the faculty of the new school was largely recruited from that of the Fairfield School. It was possible in those days, due to the shortness of the annual sessions, for a professor to follow the example of the peripatetic professor of the Middle Ages, and hold as high as five chairs in five different schools, and not all of them the same chair either. While they were giving their lectures in Willoughby, these teachers "boarded around" with the good citizens of the town. Later there came several from the Berkshire Medical Institute. From these two schools came most of the early teachers and the ideals, more from Fairfield than from Berkshire. In general, it may be said that at the end, the Fairfield men went to Cleveland and founded the Cleveland Medical College while the Berkshire men came to Columbus. So this may have been the root of the trouble in the faculty at Willoughby as it developed through the years.

The faculty list from 1834 to 1847 contains the names of many of the outstanding educators in American Medicine.<sup>1</sup>

The faculty disagreed among themselves about many things. There was a growing local prejudice against practical anatomy and the way bodies were secured for dissection and demonstration. There were many administrative difficulties in the job of maintaining a salaried faculty in residence only during their own course. The professors and trustees discussed for some time the advisability of changing the location to a larger center of population as it became increasingly clear that Cleveland, and not Willoughby, was destined to be the metropolis of northern Ohio. Meantime, several of the faculty already lived and practiced in Cleveland. These naturally wanted to move the college to Cleveland, others did not.

In 1843, Delamater, Kirtland, Ackley, and Cassels resigned with the intention of organizing a school in Cleveland. This was done upon the gift of land and a sum of money. This was the beginning of the present day Western Reserve University School of Medicine.

Those who were left began to plan for the future of the school at Willoughby. Dr. John S. Butterfield, the man who was imported from the East upon the resignation of the Cleveland group for the chair



Fig. 2 The Wesley Chapel used for recitations and lectures by Willoughby Medical College of Columbus, Ohio

of medicine, soon decided that the thing to do was to move the school to the rapidly growing capital of the state. Working with Dr. Richard L. Howard, Columbus' first surgeon, he was able to do this. By act of the Ohio legislature the charter was amended accordingly, and The Willoughby Medical College of Columbus with a separate board of trustees came into being. It opened its doors for instruction on the seventh day of October, 1846. This session was held in a large frame building which had been moved from State Street to the northwest corner of Gay and High Street and remodeled into a small anatomical room and amphitheater with a seating capacity of 150. The next year additional room was secured by the rental of the basement of the Wesley Chapel a half block north. The faculty was composed of Henry Halsey Childs of Massachusetts, John Butterfield from Willoughby, now of Columbus, T. Rush Spencer of New York, also of the Willoughby faculty. The new teachers were Richard L. Howard of Columbus, Samuel M. Smith and Jesse P. Judkins of Cincinnati, Frederick Merrick of Delaware, and Norman Gay of Columbus.

It has been said that Lynn Starling, one of the founders of Columbus, was interested from the beginning in getting this school for his city and that he made a visit to Willoughby for the purpose of setting forth the advantages of Columbus. Thus we have not been able to verify. At any rate, the school and Starling's relatives, friends, and personal physician took a prominent part at once in its organization and direction. On December 18, 1847, Starling made a gift of thirty thousand dollars to the medical school on condition that *it would establish a hospital in connection with the school for the sick poor*. At a later date he added five thousand dollars more to his bequest.

<sup>1</sup>Horace A. Ackley, John Cook Bennett, T. W. Donovan, George Jones, William M. Smith, Francis Winthrop Walsh, Samuel Underhill, George W. Card, Hoamer Graham, Storm Rosa, Daniel Levi Madara, Peivotto, John Lang Cassels, Amasa Trowbridge, Stephen West, Williams, John Delamater, Orson Swift, St. John, Jared Potter Kirtland, John S. Butterfield, Robert Hamilton Paddock, James Quackenbush, Isaac J. Allen, Henry Halsey Childs, George McCook, Abner Hartwell.

Brown, Thomas Rush Spencer—these were the men who served at Willoughby. A number of them had long before established their claims to be regarded as men of high attainments—having been public teachers in our first medical schools of that day. The reader is referred to Frances Packard's *Medical History of the United States of America* for the details of the part that these men took in the other American medical schools of the time.



Fig. 1. The Starling Medical College and Hospital.

When the changes consequent upon Mr. Starling's donation had been completed, by vote of the trustees and faculty the name of the school was changed from the Wiloughby Medical College of Columbus to the Starling Medical College. Mr. Starling had not asked for such change nor was it known that he expected it, but he accepted. So the Starling Medical College opened its first session with a new charter incidentally to receiving the gift of \$30,000 which up to that time was the largest gift that any citizen of Ohio had ever made to any institution. It was to the same building with the same equipment and the same Dean and faculty with the addition of Dr. Francis Carter. There was, then, a strict continuity of work, purpose and personnel. Upon these facts, the College of Medicine of the Ohio State University rests its claim that it is now in its one hundred and first year of teaching.

The frog-pond full of malaria on East State Street was purchased, largely because the citizens, almost to a freeholder objected to having a medical school near their property. Plans were submitted by various architects. That of the present edifice of St. Francis Hospital, drawn by M. R. H. Sheldon of New York, proved the most attractive. The estimated cost strangely enough was \$35,000. This left nothing for endowment or equipment. The plans, however, are so attractive that the trustees decided to go ahead and build. That proved to be the outstanding piece of architecture in the city and one of the finest of its type in the country.

The cost of the building turned out to be nearly twice the estimate. Thus the institution which started with a larger sum of money than any other medical school in the State was by the fourth year of its existence handicapped by debt which constantly absorbed the greater part of its income until '87. In 1833 the hospital part completed and

opened for patients. In 1834, private apartments or completed nicely furnished and set apart for the special accommodation of females, who resort to them for the treatment of diseases peculiar to their sex. This plan of having a hospital in connection with medical school seemed and controlled by its trustees was years ahead of the times. In '35, the wards of the Ohio Penitentiary with its sick cell of 3 to 60 patients per day was opened by legislative act to the medical students for their instruction.

In '34, for reasons now obvious, the principle of a resident faculty was adopted in order that the teacher must devote a part of his time throughout the year to the development of the school. This new principle, of course, did away with the salaried lecturers from Pittsfield and Buffalo.

The history of the school now parallels that of other medical colleges in this country. Although attendance fell off, standards were raised and the instruction given was thoroughly adequate and as comprehensive as the development of medical science permitted at the time. The reputation of the local teachers grew and the school prospered. When the war between the states broke out, medical education in the United States was conducting itself upon a very high plane—higher than it was ever able to reach until after the Flexner report in 1909. With its well known and respected faculty, its own hospital, and its adequate equipment, the Starling Medical College occupied most honorable position among American medical colleges.

The first outstanding contribution to medicine to come from the Starling Medical College was some twenty papers and finally in 1867 the *As* magazine of Dr. T. G. Wormley who at that time was professor of chemistry and toxicology. This work was an elaborate chemical and microscopical analysis of the nature and operation of many different poisons. It



Fig. 4. The Ohio Medical University and Protestant Hospital.

was the result of patient experimentation and cost the lives of some 2,000 cats and dogs

In addition to Dr Wormley, Dr Starling Loving stood out in medicine and Dr John Hamilton in surgery. These men were not only great teachers but great clinicians

From 1857 to 1875 there were "few important changes and the classes gradually increased to respectable numbers." In 1875, the debt on the buildings was paid off and trouble started. Professors J W Hamilton, D N Kinsman, H G Pearce, and David Halderman, resigned and organized the Columbus Medical College. The effect of the simultaneous resignation of so many well known teachers, the founding of a rival school, and the addition of several new and untried men to the faculty, all served to diminish greatly the attendance. By 1879, however, the confidence of the profession and of the public had been in a large measure regained. From that time on the attendance was large and the college prospered

#### THE COLUMBUS MEDICAL COLLEGE

For seven years, this college was conducted in the Session's Block on High Street. In January, 1882, it was transferred to a commodious college building on Long Street, which was especially constructed for the school

On March 3, 1882, Dr W B Hawk donated to this college four lots on the west side of the river and \$10,000 for the erection of a hospital. About \$10,000 was added to the original donation and an elegant hospital was erected in 1886. Thus began the Hawkes Hospital of Mt Carmel

The Columbus Medical College had a strong faculty and during the seventeen years of its existence it graduated about five hundred students

In 1892, the Columbus Medical College suspended its operations as a separate teaching body and went back into the Starling Medical College

#### THE OHIO MEDICAL UNIVERSITY

Certain of the teachers of the Columbus Medical College who did not return to the Starling Faculty joined with others in the organization of the Medical Department of the Ohio Medical University. This department together with those of Dentistry and Pharmacy began its first session on September 7, 1892, in a residence property at 775 North Park Street. At its inception the Ohio Medical University adopted the recitation plan of instruction and gave laboratory work and clinical medicine a prominent place in the course of instruction

A lot was soon purchased and a university building, specially planned for its purposes, was erected on Park Street opposite Goodale Park

In 1893, an agreement was entered into between the trustees of the Protestant Hospital, then occupying the present Radium Hospital, and the trustees of the Ohio Medical University by which the faculty of the school was to have exclusive charge of the clinical material of that hospital. The University donated the lot adjacent to the hospital on the south, and \$5,000 to aid the erection of the hospital building which was completed in 1898

The trustees purchased the lot adjoining the University on the north and erected thereon, in 1896, a large building for laboratory purposes

In 1898, they erected another four-story structure facing the park. It has a modern gymnasium and bath rooms in the basement and a large assembly hall on the fourth floor. This building greatly enlarged the facilities and added to the architectural appearance of the University

These institutions—Starling Medical College and the Ohio Medical University—at all times stood fully abreast with the best medical colleges in the West in elevating educational standards, meeting all the requirements of the Association of American Medical Colleges and the State Board of Medical Registration and Examination. They enforced the





FIG. 3. The College of Medicine, Ohio State University and its hospital

three years requirement for all students graduating from 1893 to 1895 and the four years requirement of those graduating in 1896, the four year graded course having been adopted by both colleges for all students graduating after January first of that year.

The unity of the colleges at the beginning of this century and their desire to enforce their announced requirements and to raise the standard of admission was treated by the agreement of both colleges to have a common examining committee in no way connected with either college to pass upon the credentials and preliminary education of all students.

#### THE STARTING OHIO MEDICAL COLLEGE

In the spring of 1907 negotiations were completed for the union of the Starting Medical College and the Ohio Medical University. Each school gave to own diploma to its senior class and from then on operated as single school.

During the days of the Starting Ohio Medical College, too much credit cannot be paid to Dr. William J. Means who as dean, and professor of surgery performed what to any one else would have been an impossible task. By persistence he not only accomplished the merger with the Ohio State University, but he kept a first class medical school operating from student fees as its only source of income. In those days, Dean Means was a member

of the inspection committee for the American Association of Medical Colleges. In this work he visited practically every medical college in the North America continent once every 1 year, and this in the company of such leaders as Dr. West of Western Reserve and Dr. Caldwell of the Council on Education of the American Medical Association. On return from each of these trips the good Dean would proceed to install all the ideas he had gotten which he could possibly use. Credit should also be given to the faculty who co-operated with him. With this dean at the greatest personal sacrifice much of the inspiration for this merger came from Professor Landacre and Dr. Ernest Scott.

It is obvious to those of us who are watching this literature that of competing in performance without financial help is ever increasing expenditures in other medical schools, that the limit must

soon be reached. Dr. Thompson at the time of his election as president of Ohio State University had promised to postpone the establishment of medical college until the time was ready. Dean Means was able to convince President Thompson that this was the time. The necessary legislation was secured to do this and to take over the Cleveland Public Hospital College, and so the University found itself with two colleges of medicine. With the completion of more than seven years (1914) of unremitting effort, Dr. Means was through. The same qualities which had made him a success as head of his own institution, unfitted him to lead his way about in the mass of large and now highly organized university. Like the prophet of old, he led his children into the promised land, but he himself could not enter.

Dr. Eugene F. McCampbell resigned his position as the state commissioner of health to succeed Dr. W. J. Means as dean of the College of Medicine of the Ohio State University. He set himself to the task of effecting a complete reorganization of the faculty along acceptable university lines. The number of the members of the faculty was cut nearly in two. Entrance requirements continued to be raised. Here it was again men like Drs. Landacre and Scott who gave the necessary support to these seemingly radical changes. Dr. Landacre accepted the chair of anatomy on condition that the department be put on a proper university basis, with recognition of the importance and scope of anatomy as science and not merely as a necessary part of the professional training of physicians. Both of these interests Professor Landacre guarded zealously although it meant that he himself must assume the double load of teaching and the administration of both comparative vertebrate anatomy and human histology. The event has justified his decision and the enormous labor which, during all these subsequent years, has been directed toward its realization by Dr. Landacre and loyal associates whom he had trained and inspired with his own ideals. As great as his contributions were, as administrative and teaching head of the department, and his careful work as secretary of the college faculty, it was, however, the high quality of his research that made him a inspiration to all. His

passing marked the fruition of a movement in the development of comparative neurology, which the world recognized as largely directed by his hand. His outstanding original contribution was an embryological analysis of the ganglia of the cranial nerves, with an exact and well controlled account of the origin and development of their components. Dr Charles Judson Herrick of the University of Chicago, in his appreciation of the man, has recently written

His life was devoted to the Ohio State University, the intensity of this devotion and the immense labor and personal sacrifice by which he expressed it, have rarely been equaled. So quietly and modestly were his ideals of university standards of policy and practice advocated and enforced, that few people perhaps even in his own community realized their illustrious quality and the influence which he has actually exerted in shaping the course of medical education in American universities. He engaged in no propaganda. He wrote no papers. He made no speeches about medical education. He gave a practical demonstration of how it should be done and this was not done in a corner.

Dr Ernest Scott, who for thirty years occupied the chair of pathology in this college, contributed more than any one man to the success of the school in those days. He was sympathetic and stimulating with the individual student. To both the student and his colleagues, his entire efforts and extreme honesty were an inspiration. These qualities he gave to the school at great personal sacrifices, and thereby contributed a major part to blending the medical college into the life of the university as a whole.

Dr McCampbell came to the deanship excellently prepared for the job before him. No sooner had he reorganized the faculty, than he began to lay the plans for a group of medical buildings on the campus. Characteristic of the man, he accomplished his task and Hamilton Hall and the Starling Loving Hospital at Neil Avenue stand as a monument to his labors. His success marked the passing of the College of Homeopathic Medicine.

After every period of material expansion, there must follow a period of internal growth, and so that servant of the American Medical Association, for years a member of its board of trustees, Dr J H J Upham, was chosen to be Dr McCampbell's successor as dean. Objectives were consolidated under his leadership. The Department of Experimental Medicine and Surgery was established and manned by distinguished scientists.

Ohio State is proud of the hundred years of progress in its College of Medicine. Ohio State has a noble heritage which she views with pride and in humility as she begins the new Century.

Acknowledgment is made for the liberal use of material from the *History of the College of Medicine of the Ohio State University*, recently published by a committee of which this author was chairman—and from which the accompanying cuts were borrowed.

#### APPENDIX

Out of this century of progress there have come certain outstanding contributions to American medicine. They are—

- 1 DR T G WORMLEY's work on poison (1869)
- 2 DR J W WRIGHT—who first invented the intracapsular enucleation of the lens for cataract by expression (1884)
- 3 DR T D GILLIAM—who brought forward the basic method for uterus suspension by means of the round ligaments (1900)
- 4 DR JAMES FAIRCHILD BALDWIN—who presented in 1904 what is now known as the Baldwin operation. A method for the formation of an artificial vagina in the case of the absence of that organ (1909)
- 5 DR FRANCIS LEROY LANDACRE—a lifetime of research devoted to an embryological analysis of the ganglia of the cranial nerves (1900-1934)
- 6 DR ROY GRAHAM HOSKINS—series of papers on the adrenal gland which prove that its secretion is not necessary for the maintenance of a normal blood pressure (1911)

# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

THE publication of a second edition of Codman's *The Shoulder*<sup>1</sup> gives an opportunity to draw attention to something unique in medical books and to recommend a volume that should be in the library of every surgeon and practitioner who deals with injuries about the shoulder. Besides being a valuable contribution to a poorly understood subject, it is pervaded with the sincere and purposeful personality of the pioneer in this field. It is more than a dry textbook of scientific observations. It attacks one of the fundamental problems of present day surgery—the failure of surgeons to follow through cases of such injuries to determine the final end-results and the value of the various methods of treatment. It would naturally be expected that Dr. Codman would emphasize this problem, for all his life he has fought for the principle of "evaluating the end results of surgery."

The preface and epilogue of the book, in addition to being most readable, are enlightening and stimulating as the philosophy of the inquiring mind. As the American College of Surgeons adopted and fostered his earlier advocacy of analyzing "End-Results" he has addressed his remarks to its fellows.

Dr. Codman's early contribution upon subacromial bursitis still stands as a classic in surgical literature, and his present study of rupture of the supraspinatus tendon has aroused our interest, clarified a new entity, and if he succeeds, as undoubtedly he will, in making the general profession realize the importance of these injuries, he will have restored many patients threatened with life-long disability to comfort and efficiency—to say nothing of the hundreds of thousands of dollars he will save for casualty companies.

To make the profession shoulder conscious, Dr. Codman advocates that all hospitals make, for time, a combined study of the shoulder. Internists especially should have their attention focused on the lesion, and all cases of shoulder injury not recovering promptly should be presented at staff conferences. He is right in believing that this will result in time in prompt recognition of obscure lesions and the institution of early proper treatment by which the present inadequate and costly care may be avoided. Dr. Codman pleads for the same treatment to be applied in any contribution dealing with new principles or innovations so that an early evaluation may be secured. Hospital staffs should be proving

grounds. Thus the efficiency of hospitals would be elevated and proven procedures be made promptly available to the profession.

The various chapters cover the anatomy, normal motions and pathology in general and consider specifically arthritis, bursitis, rupture of tendons, deposits in the joint, tendinitis, brachial plexus paralysis, neuritis, malingering, tumors, and similar subjects. Dr. Codman's technique of treatment is exhaustively treated with appropriate case reports and illustrations—a contribution of 500 pages all worth reading.

THE fifth edition of *Diseases of Women*<sup>2</sup> shows considerable revision and improvement. Like previous editions, it is a collective effort of ten of the leading gynecologists of England. It is simply and tersely written and is unusually well illustrated. It should be a valuable work for students in gynecology including as it does, a complete section on the principles of technique of gynecological surgery.

The chapters on ectopic pregnancy are well written and there is an excellent and important chapter on chronic ill health from the psychological standpoint, neurasthenia in relation to pelvic disorders, a subject that American textbooks might do well to include.

The discussion of ovarian functions and the entire discussion of the endocrines have been brought up to date. These sections are exceptionally well written, as is the one dealing with the disorders of menstruation.

The American gynecologist will disagree with the liberal use recommended for the uterine sound, the methods for the examinations of the discharge, and the fact that anesthesia is still recommended for the Rubin insufflation test. In this edition the use of the electric cautery in cervical disease is included for the first time. However the pleasing and informal style in which the entire book is written, together with the fact that it presents an accurate picture of British gynecology of today should make this volume a desirable addition to the gynecologist's library.

RAULF A. RICH.

RECENTLY there have been published a number of small monographs which have dealt with the description of series of intracranial tumors of

DISEASES OF WOMEN. By Ten Teachers under the direction of Osborn Berkeley Miles, M.D., M.C. (Cambridge), F.R.C.P. (London). PAGES (Hb.), N.E.A. (Hb.), P.C.O. Bound by Osborn Berkeley Miles, F.R.C.P. and Clifford White, 2nd ed., Baltimore, Maryland, William Wood & Co., 1924.

THE SHOULDER. Rupture of the Supraspinatus Tendon and Other Lesions. By E. A. Codman, M.D. Formerly Surgeon, E. A. Codman, 121 Boston St. Boston. Price \$2.00.

1 THE PHYSICAL AND MENTAL GROWTH OF PREMATURELY BORN CHILDREN By Julius H Hess M.D George J Mohr M.D and Phyllis F Bartelme Ph.D Chicago The University of Chicago Press 1934



# CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

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## PRELIMINARY CLINICAL PROGRAM FOR THE 1935 CLINICAL CONGRESS

A PRELIMINARY program of clinics and demonstrations arranged for the twenty-fifth annual Clinical Congress of the American College of Surgeons to be held in San Francisco and Oakland, October 28 to November 1, as prepared by the local Committee on Arrangements, appears in the following pages. It will be noted that operative clinics and demonstrations in the hospitals are scheduled for the afternoon of Monday, October 28, beginning at two o'clock and for the mornings and afternoons of each of the four following days. The clinical program, published in tentative form at this time, is to be revised and amplified during the next three months as the work of the program committee progresses. Assured of the hearty co-operation of the clinicians at the two medical schools and twenty-seven hospitals that will participate in the clinical program, the Committee plans to provide a program of surgical clinics in the hospitals and schools of that great medical center on the Pacific coast that will present a complete showing of their clinical activities in all departments of surgery.

The Committee expects to develop many special features in the clinical program including: (1) Cancer clinics demonstrating the treatment of cancer by surgery, radium and X-ray, (2) fracture clinics demonstrating modern methods of treatment, (3) clinics in traumatic surgery demonstrating the newer methods of rehabilitation of injured patients by surgery and physiotherapy.

The sub-committee in charge of the section on surgery of the eye, ear, nose, and throat in addition to arranging for a series of ophthalmological and otolaryngological clinics and demonstrations in the hospitals and medical schools, is preparing programs for scientific sessions at headquarters on Tuesday, Wednesday, Thursday and Friday mornings at which distinguished specialists in these branches of surgery will present and discuss papers on subjects of clinical interest.

### EVENING MEETINGS

Programs for the series of five evening sessions is being prepared by the Executive Committee of the Board of Regents. The presidential meeting on Monday evening will be held in the Municipal Opera House at which the retiring president, Dr. Robert B. Greenough, of Boston, will deliver the annual address. Officers elected at the 1934 Clinical Congress are to be inaugurated—Dr. Donald C. Balfour, Rochester, president, Dr. Arthur W. Allen, Boston, and Dr. John A. Gunn, Winnipeg, vice-presidents. At that session Dr. George Crile, of Cleveland, will deliver the American College of Surgeons oration on surgery. On Tuesday, Wednesday and Thursday evenings the sessions will be held in the Auditorium of the Veterans' Building at which eminent surgeons of the United States and Canada, together with visiting surgeons from foreign countries, will present papers dealing with surgical subjects of timely importance. On Friday evening the annual convocation will be held in the Municipal Opera House, at which the 1935 class of initiates will be received into Fellowship in the College. Dr. Robert Gordon Sproul, president of the University of California, will deliver the Fellowship address.

### SPECIAL FEATURES

Special features of the program for this year's Congress include: (1) A conference on fractures on Tuesday afternoon, the program being arranged in co-operation with the College Committee on the Treatment of Fractures. (2) A cancer symposium on Thursday afternoon under the auspices of the College Committee on the Treatment of Malignant Diseases will present additional statistics on the cure of cancer as reported by clinicians from various parts of the United States and Canada, with a number of papers descriptive of approved methods for the treatment of cancer as developed and employed in the lead-

ing medical centers. (3) A conference on Friday afternoon dealing with many of the problems being studied by the Board on Industrial Medicine and Traumatic Surgery. All of these sessions will be held in the Gold Ballroom of the Fairmont Hotel.

Surgical motion picture films, both sound and silent will be exhibited daily at headquarters at the Fairmont Hotel. Such surgical motion picture film exhibitions have met with popular acceptance in recent years and an extensive and varied exhibit, including many new films is planned for this year's Congress.

#### THE CLINICAL CONGRESS AND A VACATION TRIP TO THE PACIFIC COAST

In planning to attend the Clinical Congress in San Francisco this fall, the natural suggestion is to make this a vacation trip, the advantages of which will appeal to the Fellows of the College and their guests. The railways offer very low round-trip rates, with liberal stopover privileges, from all parts of the United States and Canada, with the added privilege of traveling to the coast by one route and returning via another affording unusual opportunities for taking many points of interest enroute.

Few cities have so impressive a setting as San Francisco. The rugged hills upon which it is built, the Golden Gate, Mt. Tamalpais, the misty bay, to the east, Oakland and Berkeley and the hills beyond all contribute to its grandeur. It is a pleasing picture and the citizens of San Francisco have not been unmindful of it. Their parks and residence districts have a dignity and beauty in keeping with the scene about them.

The glamour of the city is incalculable but no amount of description can picture accurately this unique city. One must see for himself how the many charming aspects of San Francisco and its environs blend into one delightful and unforgettable picture.

While on the coast one will naturally wish to see as much of the coast as possible and will find it surprisingly easy to "hit the high spots" in a relatively short time and at a reasonable cost. A round trip ticket at low summer rates permits one to hit scores of interesting points on the Pacific coast by having the ticket read via one route on the western trip and another route for the return trip.

Along the Pacific coast one will find much to claim his attention. First, there is the California-Pacific International Exposition at San Diego—a World's Fair of magnitude, with many important medical and other scientific exhibits—erected

in Balboa Park, a tropical fairyland. The buildings, which are permanent structures, have their dignity and beauty enhanced by the gorgeous setting.

Los Angeles with its mountain background, its broad boulevards, its nearby beaches, its hospitality—and Hollywood—afford opportunities for entertainment and recreation. A one-day trip to enchanting Catalina Island with its balmy south sea island atmosphere naturally suggests itself.

A ride through the San Joaquin Valley to the Yosemite, sublime at all times, but with autumn coloring will be unforgettable. Del Monte and Pebble Beach on the famous seventeen mile drive are but a short distance from San Francisco. Other nearby points of interest are Paso Robles, with its almond groves, lovely Santa Barbara with its famous Old Mission, and a score of cities whose names are associated with the romantic Spanish period—a fairyland of natural and cultivated beauty.

To the north there are many cities to claim your attention. Vancouver in British Columbia, built up against mighty mountains with a primeval forest almost at its environs. Seattle the great shipping center of the northwest, with Puget Sound to the west and beyond it the white-capped Olympics. In the distance the Cascade Mountains and looming to the southeast, Mt. Rainier held in special veneration by the Indians as the mountain that was God—no peak in the United States is so majestic. Portland, famous for its natural beauty—a literal bower of roses. The blue miracle of Crater Lake. Mt. Shasta and Mt. Lassen, the only active volcano in the United States.

No matter what route one takes he will view a truly great and inspiring American scene—the thriving farm lands of the midwest, the noble stretches of prairie, the sublime mountain ranges of the Rockies, the grandeur of the desert, the towering forests of the far west, and then the blue Pacific.

This year one will travel in comfort and luxury undreamed of a short time ago. Whatever route one travels he will find his train air-conditioned. This single factor adds so much to the comfort and pleasure of a transcontinental journey that it definitely and certainly marks the beginning of a new era in transportation history.

#### HOSPITAL CONFERENCE

The annual hospital conference will open the Congress with a session in the Gold Ballroom of the Fairmont Hotel at 1 o'clock on Monday morning. An interesting program of papers round

table conferences and practical demonstrations dealing with problems related to hospital efficiency is being prepared for sessions to be held on Monday, Tuesday, Wednesday and Thursday in the Gold Ballroom of the Fairmont Hotel, and at several of the hospitals. A greatly increased interest on the part of surgeons in both the administrative and scientific phases of hospital work has been evidenced in recent years and the program for this year's conference will be unique in providing for discussions of subjects of interest to the three major hospital groups—medical, surgical and administrative. It is planned to make this year's program of wide interest and practical character through a careful selection of subjects to be presented and discussed by surgeons and hospital executives, particular emphasis being directed toward professional standards and the vital problems related to medical economics.

#### HEADQUARTERS—TECHNICAL EXHIBITION

Headquarters for the Congress will be established at the Fairmont and Mark Hopkins hotels. At the former the Terrace Ballroom and Lounge, the Gold Ballroom and other large rooms on the main floor and on the terrace have been reserved for scientific sessions and conferences, registration and clinic ticket bureaus, bulletin boards, exhibits, executive offices, etc. The Peacock Court and Room of the Dons at the Mark Hopkins will be utilized for various scientific sessions.

The Technical Exhibition, including the registration and clinic ticket bureaus, will be located in the ballroom and lounge on the terrace floor of the Fairmont Hotel. In these rooms will also be found the bulletin boards on which the daily clinical program will be posted each afternoon. The leading manufacturers of surgical instruments, X-ray apparatus, operating room lights, hospital apparatus and supplies, ligatures, dressings, pharmaceuticals and publishers of medical books will be represented in this exhibition.

#### ADVANCE REGISTRATION

The hospitals and medical schools of San Francisco and Oakland afford accommodations for a large number of visiting surgeons, but to insure against overcrowding, attendance at the Congress

will be limited to a number that can be comfortably accommodated at the clinics—the limit of attendance being based upon the result of a survey of the amphitheatres, operating rooms, and laboratories of the hospitals and medical schools to determine their capacity for visitors. It is expected, therefore, that those surgeons who wish to attend the Congress will register in advance.

Admittance to all clinics and demonstrations will be controlled by means of special clinic tickets, which plan provides an efficient means for the distribution of the visiting surgeons among the several clinics and insures against overcrowding, as the number of tickets issued for any clinic will be limited to the capacity of the room in which that clinic will be given.

A registration fee of \$5.00 is required of each surgeon attending the annual Clinical Congress, such fees providing the funds with which to meet the expenses of the meeting. To each surgeon registering in advance a formal receipt for the registration fee is issued, which receipt is to be exchanged for a general admission card upon his registration at headquarters. This card, which is non-transferable, must be presented in order to secure clinic tickets and admission to the evening meetings.

#### SAN FRANCISCO HOTELS AND THEIR RATES

In addition to the two headquarters hotels—the Fairmont and Mark Hopkins—there are a number of first-class hotels within short walking distance of headquarters providing ample hotel facilities at reasonable rates. The following hotels are recommended by the Committee.

	Minimum Rate with Bath	
	Single	Double
Bellevue, Geary and Taylor	\$3.00	\$4.00
Californian, Taylor and O'Farrell	3.00	4.50
Clift, Geary and Taylor	3.50	5.00
El Cortez, Geary near Taylor	3.00	4.50
Fairmont, Mason and California	3.50	5.00
Gaylord, Jones near Geary	3.00	4.00
Mark Hopkins, Mason and California	3.50	5.00
Palace, Market and New Montgomery	3.50	5.00
Plaza, Post and Stockton	3.00	4.00
Sir Francis Drake, Powell and Sutter	3.50	5.00
Stewart, 353 Geary	2.50	4.00
St. Francis, Union Square	3.50	5.00



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Franklin Hospital—FRANK GYRELLA, LEON BROOKS  
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Littleton General Hospital—R. T. METCALFE  
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St. Mary's Hospital—THOMAS F. MULLEN, PHILIP ARNOTT, DANIEL SOON

San Francisco Hospital—STANFORD UNIVERSITY SERVICE, LEO ELLINGER, H. MATTHEWS, L. ROODER, University of California Service, HAROLD BRIDAY, C. LAYNER, CALVERT, GEORGE K. RICHARDS

Shriners Hospital for Crippled Children—STEELE H. HARRIS, Southern Pacific General Hospital—WILLIAM WARDNER, FRANK R. GORDON

Stanford University Hospital—EMILE HOLMAN, PHILIP K. GILMAN, FREDERICK RICHMOND

Stanford University School of Medicine—LEON CRANFORD, FRANK RICHMOND

United States Marine Hospital—MARK J. WHITE, RICHARD L. W. OR

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University of California Medical School—L. WILSON, PORTER, WALLACE TERRY

Veterans Administration Hospital—P. E. JOHNSON, BILLY H. HENNING, JOHN A. KENNEDY

## SAN FRANCISCO—SURGERY OF THE EYE, EAR, NOSE AND THROAT

French Hospital—EDWARD C. PARKER, RICHARD VAYON, W. S. KILGORE

Hospital for Children—GEORGE HILGORD  
Littleton General Hospital—L. K. SCHLASSER, H. C. MAYER

Mary's Help Hospital—H. W. J. M. C. WYSON  
Mount Zion Hospital—FRANK RICHARD, HENRY CONY, FRANK HILGORD, CONY, BARTON, ALBERT

St. Joseph Hospital—ROY PARLINSON

St. Luke's Hospital—WILLIAM E. LINDSTROM, C. ALLEN BATES

St. Mary's Hospital—FRANK CONY, S. WILSON, BILLY BROWN

Southern Pacific General Hospital—WILLIAM SWETT  
Stanford University Hospital—FRANK S. PELL, H. BARKER, HARRINGTON, C. WILSON, LEO MORRISON

United States Marine Hospital—R. S. HILGORD  
University of California Hospital—W. WALLACE TERRY, FRANK C. CONY, ROBERT C. MARTIN, C. ALLEN BATES

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# PRELIMINARY CLINICAL PROGRAM

GENERAL SURGERY, GYNECOLOGY, OBSTETRICS, ORTHOPEDICS, UROLOGY  
SURGICAL PATHOLOGY, ETC

## OPERATIVE CLINICS IN SAN FRANCISCO HOSPITALS—DAILY

### SAN FRANCISCO HOSPITAL

*University of California Service*

- HAROLD BRUNN, GEORGE K. RHODES, A. R. KILGORE,  
C. I. CALLENDER, S. H. MINZLER, A. I. BROWN,  
H. W. STEPHENS, F. S. LOOTH, M. W. DEBENHAM,  
H. M. BLACKFIELD and I. GOLDMAN, General surgery  
T. HINMAN, C. JOHNSON, S. OLSEN, J. HAYES, J. J. SULLIVAN, W. A. CALVERT and T. O. POWELL, Urological operations  
W. G. MOORE, A. M. VOLLMER and M. SCHULZ, Gynecological operations  
H. W. ELKINS, H. A. BROWN and I. B. LAWRENCE, Neurosurgical operations  
FREDY ARNOTT, I. G. HEDGECOCK, R. C. BOST, W. J. COX and K. O. HALDEMAN, Orthopedic operations

*Stanford University Service*

- I. ROELOFFSE, Lobectomy for lung tumor, ship operation for tuberculous empyema, disarticulation at knee joint  
W. I. REEVE, Apicectomy (paraffin fill)  
J. M. MEHRIN, Gastric resection (Billroth I)  
EDWARD BUTLER, Pyloroplasty for peptic ulcer, atresia of colon congenital  
J. CLAY, Exploration of biliary duct  
C. MATHISON, Open reduction of spiral fracture of the tibia, sequestrectomy for tuberculosis of the pelvis  
D. K. C. Nonunion of carpal scaphoid  
M. R. OTTE, Resection for carcinoma of the colon  
I. TOWSE, Laminectomy for decompression of cauda equina  
E. MORRISSEY, Removal of cord tumor  
I. RYNNOLDS, Cystectomy for carcinoma of the bladder  
G. HARTMAN, Suprapubic prostatectomy  
I. MICHAELSON, Plastic on kidney pelvis  
R. CRAIG, Nephrectomy  
K. SCHULZ, Removal of fibromyoma of the uterus  
A. PETTIT, Vesicovaginal fistula  
H. VOEGELIN, Perineal repair operation  
C. COOLEY, Operation for pelvic inflammatory disease  
R. DUNN, Hyam's conization of the cervix  
D. DALLAS, Vaginal hysterectomy

### UNIVERSITY OF CALIFORNIA HOSPITAL

- HOWARD C. NAFFZIGL, D. JONES, JR., H. BROWN and R. AIRD, Neurosurgical operations  
HAROLD BRUNN and H. STEPHENS, Thoracic surgery  
R. ABBOTT, F. BOST, K. HALDEMAN and W. KEYS, Orthopedic surgery  
A. MAXWELL, M. SCHULTZE, D. MORTON and C. HAYDEN, Gynecological and obstetrical operations  
FRANK HINMAN, C. JOHNSON, S. OLSEN and B. WAYMAN, Urological operations  
W. S. TERRY, General surgical operations, thyroidectomy  
H. SEARLS and H. GLENN BELL, Carcinoma of colon, cholecystectomy, popliteal aneurysm  
C. ROSSIN, Appendectomy, hernioplasty  
M. S. WOOLF, Carcinoma of rectum and lower bowel  
F. FOOTE, Partial obstruction, new operations  
F. O. BAPTIST, Carcinoma of breast

### STANFORD UNIVERSITY HOSPITAL

- EMMET RINCHORD, EDWARD BUTLER, R. GILMAN, L. CHANDLER, EMILY HOLMAN and S. BUNNELL, General abdominal surgery, gastro-intestinal surgery, hernias  
EMILY HOLMAN and H. LOESSER, Thoracic surgery  
F. REICHERT and L. TOWNE, Neurosurgical operations  
R. GILMAN, EMMET RINCHORD, EMILY HOLMAN, Thyroid, biliary tract, liver and pancreas surgery  
A. L. FISHER, D. KING and M. MINOR, Orthopedic operations  
J. DILLON and L. RYNNOLDS, Urological operations  
I. MACE, H. A. STEPHENSON, C. FLECHMAN, P. I. HOFFMAN, G. CRAIG and W. STEVENS, Gynecological and obstetrical operations  
I. REICHERT and EMILY HOLMAN, Cardiac conditions, circulatory diseases  
C. B. PALMER and R. B. FRAVON, Injections, anesthesia  
R. A. SCARBOROUGH, Proctological operations  
A. DAVIS and S. BUNNELL, Plastic surgery, industrial cases, skin diseases

### MOUNT ZION HOSPITAL

- HAROLD BRUNN, Total thoricoectomy for cardiac disease  
I. I. HARRIS, Tork operation for undescended testicle, first and second stage procedures, resection for lesions of descending colon, radical mastectomy, Pexcautery and endotherm  
A. I. BROWN, Plastic repair of pendulous breasts, herniotomy  
W. WALDMAN, Appendectomy  
M. GROFFER and A. WHITE, Blood transfusion, citrate, Underman and Unger methods  
L. HOFFMAN, Hysterectomy  
L. D. PRINCE, A. SIRBU and DAVID CHARMAN, Radical clavectomy, fracture of os calcis  
H. BLACKFIELD, Plastic correction of congenitally protruding ears  
HAROLD BRUNN and A. I. BROWN, Phrenic avulsion, thoricoectomy  
A. ZOBEL and D. A. SUSNOW, Electrocoagulation of tumors of the rectum, hemorrhoidectomy under local infiltration  
L. C. JACOBS, Calculi of the urinary bladder, transurethral prostatectomy  
H. A. R. KRUTZMANN, The problem of urinary lithiasis, nephrotomy, pyelotomy, nephrectomy  
B. STRAUSS and M. POISE, Hydrocele operation, plastic operation for phimosis, cystoscopy  
A. EPSTEIN, Injection of vas deferens for chronic epididymitis  
R. K. SMITH, Classical cesarean section  
A. BEERSTEIN, Demonstration of cervical repair immediately following delivery  
F. PEARL, Muscle splitting extrapentoneal lumbar sympathetic ganglionectomy, a new approach, muscle splitting posterior cervicodorsal sympathetic ganglionectomy  
EDWARD H. BOLZE, HERBERT H. SCHULTZ and DR. LAZAR, Demonstration of introduction of anesthesia by avertin, evipal, gas and oxygen, spinal

## ST MARY'S HOSPITAL

- T. E. BAILEY. Gastric surgery; gastrectomy  
 ROBERT L. OELL. Gall-bladder surgery; cholecystectomy  
 D. BOOT. Surgical intervention for duodenal ulcer  
 C. P. MATHE. Nephropathy for nephropathy  
 E. TOWMAN. Inguinal hernia  
 JAMES MCCARTHY. Industrial emergency cases  
 EDWARD BUTLER. Surgery of the colon  
 GEORGE K. RICHARDS. Emergency surgery  
 EDWARD MORGAN. Sympathectomy for Raynaud's disease  
 PHILIP ARNOY. Obstetrical surgery  
 T. GIBSON. Nephrectomy  
 W. FACHNER. Bronchoscopic diagnosis of lung abscess  
 J. LOOTENBERGER. Out treatment for delayed berry infection.

## LETTERMAN GENERAL HOSPITAL

- R. F. MITCHELL. Cauterization of cervix, perineorrhaphy  
 suspension of uterus; gastropylorostomy; cholecystectomy  
 hemiorrhoidectomy; oesophagomy for rectal carcinoma, cesarean section  
 F. L. COLE. Hernia; appendectomy; inguinal hernia  
 cystic hernia  
 H. S. BLUM. Gynecological operations; electrical resection  
 B. S. BURKE. Thoracotomy for empyema, orthopedic  
 operations; bone graft; open reduction of tibia in  
 cases of cartilage, knee  
 P. E. DOWNS. Cartilage and insertion of Carotid primary  
 for stenosis

## ST JOSEPH'S HOSPITAL

- ALVIN R. KILGORE, J. M. MURPHY, F. SEXTON and C. E.  
 SMITH. General surgical operations  
 R. BOTO-HALL and E. HALLMAN. Orthopedic operations  
 E. MORGAN. Neurological operations  
 H. VON GELDER. Gynecological operations  
 T. GIBSON. Urological operations

## FRENCH HOSPITAL

- F. A. LOWE. Fractured humerus, lateral dislocations  
 of knee joint  
 G. W. PIERCE and G. O'CONNOR. Removal of nasal bone,

## MARY'S HELP HOSPITAL

- R. MILLER. Radical neck dissection  
 L. CARLSON and C. C. McCRAE. Abdominal operations  
 M. MENON and L. PARKER. Orthopedic surgery  
 M. V. CRI. Urological operations  
 H. VON GELDER and A. SCHMIDT. Gynecological and  
 obstetrical operations

## HOSPITAL FOR CHILDREN

- C. HOWE. Thyroidectomy  
 MORRIS E. EDWARDS. Thyroglossal duct cyst  
 ALAN PERKINSON. Supravaginal hysterectomy total  
 hysterectomy; sigmoid plastic

## VETERANS ADMINISTRATION

- SUND. Colley operation for carcinoma of the rectum; second  
 stage gastrectomy

## SOUTHERN PACIFIC HOSPITAL

- V. B. COFFEY and J. D. HUNTER. Superior cervical  
 sympathectomy for angina pectoris, moving picture  
 demonstration in natural color  
 C. MATHE and T. GIBSON. Transurethral prostatectomy  
 E. GREENWOOD. Cholecystectomy  
 F. R. GILMAN. Inguinal hernia, ambulant treatment by  
 injection  
 C. WALKER and J. BONE. Open reduction of fractures  
 OSCAR F. NOLAN and THOMAS E. GIBSON. Suprapubic  
 prostatectomy  
 W. W. WARRIOR. Thyroid surgery

## ST LUKE'S HOSPITAL

- ALAN WOOD, G. D. DUFFRAY, P. ST. CASTLEMAN, A.  
 H. ROSSIGNOL, OTTO H. PETERSEN, DR. SCHULTZ,  
 DR. BLOOM and ALBERT M. VOLLMER. General sur-  
 gical operations  
 GEORGE J. MCCREARY, RUDOLPH L. DREIER and DR.  
 COE. Orthopedic operations  
 I. P. PLATON, HERBERT D. CHALL and MILLY B. VERNON  
 Urological operations  
 J. M. HODGSON. Proctological operations.

## U. S. MARINE HOSPITAL

- ROBERT A. JONES. Excision of palmaris dorsi and rectal  
 operation; cholecystectomy and arthroplasty (Guthrie  
 tubular flap) Dupuytren's contracture  
 ROBERT L. WATSON. Inguinal hernioplasty using pedicled  
 fascial skin flaps for scrotum (Haysman) ar-  
 throplasty of the knee; excision of bilateral men-  
 iscus cartilage; hernia operation (Frost) plastic  
 neurotomy  
 FLETCHER C. STEWART. Transurethral resection of pros-  
 tate

## ST FRANCIS HOSPITAL

- G. B. O'CONNOR. Plastic surgery; Reconstruction of face  
 after burns, rib cartilage transplanted to the nose; re-  
 moval of nasal bone, cleft palate reconstruction sur-  
 gery of the head  
 W. W. WARRIOR. Thyroidectomy  
 L. R. REYNOLDS and O. NOLAN. Prostatectomy; external  
 osteoplasty

## SHIRNERS HOSPITAL

- ST. AN. L. HALL. Longitudinal osteotomy transplanta-  
 tion of muscles in paralytic stabilization of foot  
 fusion of spine; lengthening of leg, congenital dis-  
 location of hip, Sever operation for obstetrical paraly-  
 sis with transplantation of tarsus; major fusion of hip,  
 plastic operations

## FRANKLIN HOSPITAL

- E. GREENE. Gastro-intestinal surgery  
 L. BROWN. Abdominal operations  
 J. SALK, V. DILLON, W. SLOWINSKY and W. COLE. Is-  
 chemical surgery and orthopedics  
 G. W. PIERCE and O. O'CONNOR. Reconstruction surgery  
 of head, face and neck after burns; repair of eyelids,  
 correction of blepharospasm

## CLINICAL DEMONSTRATIONS IN SAN FRANCISCO HOSPITALS—DAILY

## GENERAL SURGERY

- A S WHITE and F J HARRIS Injection treatment of hernia
- HAROLD BRUNN Appendicitis
- S K SHERMAN Rupture of the spleen
- J HOMER WOOLSEY and H GLENN BEIL Splenectomy
- WALTER B COFFEY Inspection of an industrial medical and surgical center, wound rounds, demonstration of cases, postoperative treatment
- ELMER RIVKORD Knotty problems in industrial surgery
- Traumatic carcinoma of breast, ruptured heart, traumatic thrombosis of iliac and other large veins
- EMILE HOFFMAN Operative cure of recurrent and direct inguinal hernia
- GROVER A KNOTHS Hematogenous perinephric abscess, peritonitis and drainage
- M W DEBENHAM Aseptic meningitis following spinal anesthesia
- A L BROWN Pulmonary embolism, motion picture demonstration of the Trendelenburg operation on cadaver
- H BRODIE STEPHEN Subphrenic abscess, vaccination of the pleural and abdominal cavities
- WALTER HENDBALM Tendon repair, acute gonococcal tenosynovitis
- ALSON R KILGORE, OTTO H PELVICER and R S STONE Treatment of breast cancer and results
- OTTO H PELVICER Soft tissue sarcoma
- ALSON R KILGORE Cystic disease of the breast cancer
- C L CALLANDER Gas bacillus infection, new amputation of thigh in lower third, treatment of septic joints
- FREDERICK BUTLER Emergency surgery
- FREDERICK BUTLER, L R REYNOLDS, I H GARDNER and J B McVAUGH Old healed ruptured bladders, diagnostic difficulties and value of X ray in diagnosis, X ray in differential diagnosis of acute abdomen
- ELMER S KILGORE Circulatory disease in differential diagnosis of acute abdomen
- CARLETON MATTHEWS, JR and J B McVAUGH Lymphogranuloma inguinale
- A S McSANT Postoperative infections
- I W THORNT Squamous and basal cell carcinoma of face and neck, pathology, diagnosis and treatment
- Z E BOLIN Biopsies and tumor surgery, mixed tumors of the parotid
- EVERETT CARLSON Carotid body tumors, splenectomy, indications and technique
- FRANK E STILES Treatment of varicose veins
- J F RICKARD Intestinal obstruction

## SURGERY OF THE THYROID

- WILLIAM J KERR, HENRY H SEARLS, JANE T PAXSON and R S STONE Activities of the thyroid committee of the University of California Hospital with follow up studies after various lines of treatment
- HENRY H SEARLS, E I BARTLETT and C L COGNOR Chronic diffuse thyroiditis
- HENRY H SEARLS and JANE T PAXSON Clinical picture of toxic adenoma with normal or lowered metabolic rate
- WILLIAM J KERR The heart in parathyroidism
- M L MONTGOMERY Lingual thyroid
- THEODORE ALTHAUSEN Surgical implications of hepatic damage in thyrotoxicosis
- R J MILLNER Parathyroid damage during thyroidectomy

## GENITO URINARY SURGERY

- FRANK HINMAN, CLARK M JOHNSON and BRENT WILMAN Tumors of the testicle, pathology, demonstration of hormone tests and results, uretero intestinal anastomosis, experimental work, drawings and motion picture demonstration, demonstration of patients, prostatism, pathology, indications for different types of surgery, end results by different methods
- C P MATHIE Surgery of the prostate
- T I GIBSON Newer aspects of renal tuberculosis
- L P PLAYER and H D CRALL Gricilis transplantation for urinary incontinence
- MILLY B WESSON Conservative surgical treatment of nephrolithiasis
- L C JACOBS Calculi of urinary bladder, suprapubic and transurethral prostatectomy
- H V R KREUTZMA Urinary lithiasis, nephrotomy, pyelotomy and nephrectomy
- BIR and STAPLES and M I POISE Operation for hydrocele, plastic operation for phimosis
- A FERTIG Injection of vas deferens for chronic epididymitis
- J V LONARD and GEORGE W HUNTLEY Demonstration in urology
- C P MATHIE and T F GIBSON Transurethral prostatectomy
- T I GIBSON and O F NOLAN Suprapubic prostatectomy
- J R DILLON Treatment of chronic pyelitis and pyelonephritis, treatment of cancer of prostate, technical improvements in surgical treatment of undescended testicle
- W I STEVENS Unusual pathological conditions of the urinary tract in women
- IDA R POTH A new aseptic technique for uretero-enterostomy, mechanism of ascending infection of the urinary tract, experimental observations
- SIDNEY OLSEN Tuberculosis of the genito urinary tract, urinary calculi
- CLARK M JOHNSON Trauma of the genito-urinary tract, infections of the genito-urinary tract, renal and pararenal infections, renal anomalies
- L P PLAYER Kidney lavage
- W A CARROLL Ureteral lithiasis, rupture of kidney
- T O POWELL Newer knowledge of tumors of the testicle with special reference to gonadotropic hormone excreted in the urine
- M R OTTINGER, LLOYD R REYNOLDS and J B McNAUGHT Torek operation of undescended testicle, torsion of testicle
- GEORGE W HARTMAN Hematuria and pyuria, renal tuberculosis
- W A SUMNER Relationship of chronic infections to lesions of the genito-urinary tract
- LEWIS MICHELSON Obstruction of the neck of the bladder in the female
- R. GLENN CRAIG Ureteral pain of obscure origin
- MORRELL VECKI Renal movability

## SURGERY OF INFECTIONS

- A S WHITE Treatment of staphylococcus infections with staphloblind
- S A GOLDMAN Studies on staphylococcus infections
- F J MCCARTHY End results in infections of the hand
- B F ALDEN Relation of focal infection to Wassermann fast lues

## ORTHOPEDIC SURGERY

- GEORGE J. MCCORMACK, W. COX and R. L. DICKER. Fracture of neck of femur: treatment without external splinting.
- L. D. PRINCE, A. B. SMITH and D. D. CHURCHILL. Fractures of os calcis; replacement of tibial shaft by fibula following osteomyelitis: treatment of berriete.
- R. L. WATSON. Clinical demonstration of Roger Anderson "Eight O-Matic" splint and skeletal traction and countertraction methods applicable to Thomas or Hodgson splints.
- LAUREN C. ARNOTT. The shoulder joint.
- JERRY B. DE C. M. BATHURST. The shoulder joint.
- J. F. RIVERMAN. Vitamin C deficiency in arthritis.
- KENNETH HALLIDAY and JOHN B. DE C. M. BATHURST. Demonstrations of bone growth.
- FRANCIS BAKER. Heat therapy.
- F. A. LOWE. Internal derangements of knee joint, clinic and motion picture demonstration, fracture of the tibia, clinic and motion picture demonstration.
- J. J. LUTCHER. Arthrodesis of foot.
- S. L. HALL. Application of Hibbs-Kasser plaster for scoliosis: results of treatment for scoliosis, results of tendon transplantation. Legg-Perthes disease.
- J. J. BAKER, W. O. MONTGOMERY, J. M. DILLON and W. J. COX. Industrial surgery and orthopedics.
- J. H. O'CONNOR. Reduction of complicated fractures, closed methods, demonstration of cases, indications for open reduction.
- C. A. WALKER. End results of open reduction of fractures: treatment of compression fractures of spine, 50 cases; fractures of clavicle and patella.
- W. W. WALKER. V. Debridement following fractures, factors influencing period of recovery.
- LEONARD W. ELL. Arthritis of the hip.
- D. KIRBY. Functional anatomy and pathology of the shoulder joint.
- A. L. FINKE. Treatment of flat feet.
- MICHAEL C. MERRISON. Osteogenic sarcoma of spine: relation of bacteriophage to the Orr treatment of osteomyelitis.
- NELSON J. HOWARD. Traumatic lesions of bony tendons and muscles.
- LEON PARKER. Facial tendons in Paget chamber.
- D. KING. Treatment of chronic sclerosing osteomyelitis.
- F. G. LYONS. Compression fractures of spine: non union of fractures.
- F. C. BOST. Hibbs-Kasser treatment of scoliosis, dislocation of carpal scaphoid: fracture of ankle, ligamentous tears of ankle: treatment of fracture of os calcis.
- W. J. COX. Internal derangement of knee joint, rupture of ligaments, treatment of fracture of femoral neck with Smith-Petersen table.
- KENNETH O. HALLIDAY. Pathology of acute osteomyelitis, pathology of chronic infections of bone.
- RAULS SOTO-HALL and KENNETH O. HALL. Fracture dislocation of cervical spine: Drinker's traction apparatus.
- PAUL J. JOHNSON, B. H. HEN, and JOHN A. KEN. Disability ratings of Veterans: Administration for orthopedic conditions of the extremities.
- CARLETON MATTHEWSON, J. and J. R. McNAUL. Treatment of spiral fractures of tibia: open and closed methods of treatment of fractures of extremities, tuberculous of pelvis.
- D. KING, J. M. MERRISON and R. A. SCARBOROUGH. Fracture of carpal scaphoid: surgical approaches to bones and joints, Orr method of treatment of osteomyelitis.
- NELSON J. HOWARD. Fractures of the upper end of the humerus, motion picture demonstration.

- MICHAEL C. MERRISON and LEON PARKER. Unusual fractures of the spine: treatment of osteomyelitis with surgical approach.
- C. C. McRAE. Injuries of small bones of the hand.
- EDGAR L. GILCHRIST. Problems in treatment of fractures.

## THORACIC SURGERY

- HAROLD BRYAN, A. L. BROWN, H. ROSENFELD and J. J. SAMPSON. Symposium on surgery of the heart with particular reference to adrenergic pericarditis.
- LEO LLORENTE, WILFRED H. PETERSON, W. L. ROUTINE, W. C. BURNHAM, DAVID A. WOOD, W. R. CLARK and L. H. GARLAND. Various types of bronchial stenosis, serous infections of the lung: tumors of the lung: empyema.
- EARLE HOLLAND. Technical improvements in partial selective thoracopharyngeal resection of transverse process, resection of scapula, ligation of the pulmonary artery as therapeutic measure in pulmonary hemorrhage: carcinoma of lung: abscessing inflammatory disease.
- HAROLD BRYAN, SAMPSON, J. SAMPSON, H. ROSENFELD, A. L. BROWN, M. W. DIERCKMAN and A. OGDON. Lung neoplasms: empyema, artificial pneumothorax: pleural evulsion, thoracoplasty.
- ALANSON WICKER and G. D. DILLON. Thoracoplasty.
- RA. KUTLER. Diaphragmatic hernia.
- SURVEY J. SAMPSON. Pneumothorax in pneumonitis.
- W. B. FULTON, J. BROWNE, treatment of chest injuries.
- A. L. BROWN. Collapsus therapy in pulmonary tuberculosis.
- S. SAMPSON. Lymphoblastoma of mediastinum.
- C. A. WALKER. Pharyngectomy for pleuropulmonary tuberculosis.
- A. GORDON. Staphylococcal infections of the lung, chemotherapy in tuberculosis.
- T. F. MILLER. Intrathoracic esophagoplasty.
- MARY E. M. THIES. Experimental study of the effect of various pathological conditions upon the dual blood supply of the lungs.
- EDGAR FOTE. A simple apparatus for tidal and apical irrigation and transpiration in treatment of empyema.
- D. VID A. WOOD and MARY E. MATTHEWSON. Subject of clinical and experimental observations on the dual blood supply of the lungs in various pathological states.

## NEUROSURGERY

- HOWARD C. NAPPREYER. Late results in the treatment of malignant ependymomas: brain tumors: factors in obtaining recovery after peripheral nerve injury: cervical ribs and the scalenus syndrome without cervical rib.
- HOWARD W. FLEMING. Subdural hematomata, cerebral thromboses, relief of intractable pain, cranial approach for orbital tumors, craniofacial injuries.
- BROWN MORRISON. Neurologic clinic or lesions of the cauda equina: diagnosis and treatment of subdural hemorrhage, diagnosis of subdural hemorrhage.
- O. W. JONES. Spinal cord tumors.
- H. A. BROWN. Low back injuries, spinal cord injuries.
- F. B. TOWNE. Treatment of acute head injuries.
- F. L. REEDER. Neuralgia of cranial nerves, demonstration of patient and lantern slides.
- ROBERT WOOD. Encephalography: clinical and experimental intradural alcohol injections for intractable pain.
- E. B. TOWNE, E. MORRISON, J. W. WOLFE and D. WOOD. Surgical lesions of the spinal cord, dynamics of epilepsy.
- L. B. LAWRENCE. Spinal cord tumors: tumors of cauda equina.
- LEY HARR. Regeneration of peripheral nerves of hand.

# GYNECOLOGY AND OBSTETRICS

- WILLIAM G. MOORE Endometriosis, fibromyomata of uterus  
 A. M. VOLLMER Rubin's insufflation test trichomonas vaginalis  
 R. K. SMITH Classical cesarian section motion picture demonstration  
 FRANK VINCH ALICE MAXWELL and R. S. STONE Uterine cancer follow up X ray therapy radium therapy  
 MARGARET SCHULTZ Special ovarian tumors  
 A. H. HEAD and ALICE MAXWELL X ray pelvimetry, direct method  
 PHILIP H. ARNOT Conduct of labor in posterior position  
 LEONARD L. LOR Dysmenorrhea causes and treatment sterility diagnosis and treatment  
 C. F. EICHMANN, P. I. HOFFMAN and GEORGE E. JONES Endocrinological aspects of gynecology modern methods of diagnosis blood and urine hormone tests biopsy of endometrium hormone therapy  
 A. A. PETTIT Results of hyperpyrexia in treatment of acute and chronic pelvic inflammatory disease  
 EDWARD L. ELLER Radiation therapy of carcinoma of cervix methods and end results  
 A. M. VOLLMER Treatment of abortions  
 MARGARET SCHULTZ Multiple pregnancies pyelitis with pregnancy, hydatidiform mole and chorio-epithelioma cardiac disease with pregnancy  
 KAREL I. SCHULTZ Fibromyoma of the uterus  
 HANNA VON GELDERN Plastic operations on pelvis  
 C. L. COLLIER Demonstration of gynecological cases  
 R. D. DENN Treatment of incomplete abortions  
 D. A. DALLAS Operations in obstetrics  
 BEVERLY SIMPSON Separated placenta  
 ABRAHAM T. SCHULTZ Uterine bleeding

## SURGERY OF THE GASTROINTESTINAL TRACT

- HAROLD BRINN Cancer of the rectum  
 F. I. HARRIS Cicatrizing (chronic) enteritis (regional ileitis), treatment of appendix stump noninversion  
 FRED H. KRUSE The more common complications of peptic ulcer  
 E. J. BEST, F. H. KRUSE, THEODORE ALTHAUSEN and RALPH RABINOWITZ Postoperative care of intestinal conditions  
 M. F. CUNHA Primary duodenitis, end results of ulcer cases, types of operation, causes of recurrence  
 LEON GOLDMAN and THEODORE ALTHAUSEN Pseudo perforation of peptic ulcer  
 J. HOMER WOOLFE and H. GLENN BELL Carcinoma of stomach  
 M. L. MONTGOMERY and JOSEPH M. SWINDT Acute intestinal obstruction, experimental and clinical  
 H. GLENN BELL Subacute intestinal obstruction localized type (chronic cicatrizing enteritis)  
 H. GLENN BELL and LEON GOLDMAN Congenital lesions tumors, diverticula of small bowel  
 M. S. WOOLF, LEON GOLDMAN and H. GLENN BELL Carcinoma of large bowel  
 DUDLEY SMITH and J. W. MORGAN Carcinoma of rectum  
 ASA W. COLLINS Pylorotomy and gastro-enterostomy  
 LEROY BROOKS Diagnosis and treatment of intestinal obstruction  
 P. K. BROWN Peptic ulcer, indications for surgical treatment  
 W. W. WASHBURN Acute perforation of peptic ulcer, complications and end results in 100 cases

- FRANK GLIMMEL Radical surgery for gastric and duodenal ulcers diverticulitis of colon, closure of colostomy, preservation of anal sphincter  
 J. A. GUILLOT Chronic appendicitis, end results of operation  
 J. F. BOHM Mortality rate of operations for appendicitis  
 R. A. SCARBOROUGH Developments in surgical treatment of carcinoma of rectum 700 cases  
 I. M. HOLMAN Causes for failure to control symptoms and to prevent gastrojejunal ulcer in gastric surgery  
 GUNTHER W. NARL, I. I. REICHERT and MARY I. MATHEIS Chronic regional enteritis clinical experimental  
 DAVID A. WOOD Multiple primary carcinomata of colon complicating multiple polyposis of colon  
 NELSON J. HOWARD Amebic granuloma of large bowel  
 HAROLD BRINN Carcinoma of large bowel carcinoma of rectum, bowel obstruction  
 GEORGE K. RHODES Spontaneous perforation of cecum from obstruction in distal colon  
 DANIEL SOOY Choice of operation in gastric surgery  
 EDWARD THORP End results in surgery for gastric ulcer  
 H. P. HILL, GEORGE BARNETT, J. M. MEHERIN, J. W. CLINE, JR., CARLTON MATHIASON, JR., J. B. MCNAULT and A. C. MCKENNA Lesions of the upper gastro intestinal tract, amebic infections of liver and gastro intestinal tract  
 DUDLEY SMITH Operation for rectal fistula and hemorrhoidectomy, motion picture demonstration

## SURGERY OF THE BILIARY TRACT, LIVER AND PANCREAS

- ALANSON WELLS and G. D. DELFRAT Common duct stone, hydatid disease of liver, granuloma inguinale  
 I. I. HARRIS Acute cholecystitis  
 CARL HOAG Reconstruction of common duct  
 H. CLARE SHIPARDSON and HANS LIESSER Pancreatic dysfunction hypoglycemia  
 H. GLENN BELL and THEODORE ALTHAUSEN Operative mortality and pre-operative management of cholecystitis glucose therapy, Rose Bengal and other tests  
 FRED H. KRUSE and THEODORE ALTHAUSEN Medical and surgical jaundice, cirrhosis of liver, differential diagnosis from carcinoma of stomach  
 JESSIE L. CARR and FREDERICK S. FOOTH Experimental work in human jaundice  
 KARL SCHMIDT The bile salts  
 EMILE HOLMAN Postoperative and inflammatory stenosis of the bile passages  
 M. W. DEBENHAM and J. M. SWINDT Liver abscess  
 STANLEY H. MENTZER Acute cholecystitis, obstructive cholecystitis  
 ROBERT A. YOELL Gall bladder anomalies  
 T. F. MULLEN Recurrence of symptoms after biliary tract surgery

## ENDOCRINOLOGY

- R. F. ESCAMILLA Abdominal pain of endocrine origin  
 SAMUEL CORN and F. I. HARRIS Treatment of undescended testicle by operation and glandular extracts  
 LEO STANLEY Endocrinology in a penal institution

## CIRCULATORY DISEASE

- M. L. MONTGOMERY Therapeutic venous occlusion  
 C. A. NOBLE, JR. Postoperative cardiac versus circulatory collapse.

## CLINICS IN ALAMEDA COUNTY HOSPITALS—WEDNESDAY

## ALAMEDA COUNTY HOSPITAL

- WHITFIELD CRANE and W. EARL MITCHELL—g. Carcinoma of stomach  
 FRANK H. BOWLES and THEODORE LAWSON—g. Carcinoma of cervix  
 H. W. HARRIS and DON D. WEAVER—g. Carcinoma of colon  
 LEROY P. ADAMS—g. Carcinoma of breast  
 SCHWARTZ EVERTS—g. Extraperitoneal thoracoplasty; intraperitoneal pneumothorax, clinic on pleuritic infarction and thoracoplasty. Discussion by CHARLES B. SA  
 WARREN B. ALLISON—g. Neurosurgery  
 W. F. HOLCOMB—g. Arthroplasty of hip  
 L. B. BARLAND—g. Arthroplasty of shoulder  
 E. N. EWING—g. Total hysterectomy; subtotal hysterectomy. Discussion of obstetrical service at Alameda County Hospital  
 CLARENCE A. DYER—g. Gynecological cancer clinic. Demonstration of intraperitoneal alcohol injections and presentation of cases  
 ALBERT M. MIRAN, LLOYD KYEDALL, JOHN A. D. GIBNEY, T. I. BUCKLEY and associates—g. Perineal prostatic tumor; suprapubic prostatectomy; resectoscopic prostatectomy. Operations, demonstration of cases and discussion

## Dry Clinic 2—10:30

- CLARENCE A. DYER and associates. Cancer clinic  
 HAROLD H. HITCHCOCK, N. A. GARY and associates. Traumatic and orthopedic clinic, demonstration of Swensson cast dryer, Bell table, plaster models, splints, etc.  
 W. H. BARNETT and C. B. BOWEN. X-ray exhibit and discussion  
 GEORGE H. MOORE. Pathological exhibit and conference.

## BERKELEY GENERAL HOSPITAL

## Dry Clinic 9—

- FRANK D. WALKER. Cholecystitis, observations and comments on surgical treatment  
 CLAUDE H. CANNON. Ectopic pregnancy recurring on same side  
 WILLIAM W. CROSS. Polycystic kidney nephrothorax; prostatic management  
 J. F. CALHOUN. Osteochondromatosis involving all epiphyses in one extremity. Clinical drawings  
 W. W. REICH. Parathyroid disease, gross specimens and microprojections  
 R. G. VAN NORD. X-ray demonstration and discussion

## CHILDREN'S HOSPITAL

- ROY NELSON—g. Demonstration of methods of treatment of esophageal strictures due to lye  
 W. W. CROSS—g. Postnecrotic fistulas in the kidneys of children, lantern slide demonstration  
 CURTIS B. BIRNEY—g. Clinic on undescended testes. Demonstration of postoperative results. Discussion of the effect of xanthinase. Demonstration of operation

## ALTA BATES HOSPITAL

- Staff—g. Operations and dry clinics.

## SAMUEL MERRITT HOSPITAL

- WARREN B. ALLISON—g. Reconstruction of skull defects, operation and demonstration of cases  
 W. F. HOLCOMB and D. D. TOWLE—g. Orthopedic operations and demonstrations  
 MARK L. ELLIOTT—g. Rectal surgery and presentation of cases  
 FRANK H. BOWLES—g. Thyroidectomy  
 W. H. BARNETT—g. X-ray demonstration and discussion of cases  
 ROBERT A. OLIVER—g. Pathological exhibit. Demonstration of frozen section technique and specimens  
 WHITFIELD CRANE—g. 30. Peptic ulcer. Judd pyloroplasty  
 W. EARL MITCHELL—g. 30. Pelvic tumor  
 HENRY W. KOSKOFF—g. 30. Cholecystectomy  
 CHARLES A. DYER—g. Apoplexy, operation, demonstration of thoracic cases. Discussion by HAROLD TAYLOR  
 H. N. ROWELL, A. M. SMITH, W. H. STEINBERG, A. A. ALEXANDER, W. S. KUMER, STEWART V. IRVING, H. GORDON MACLEAN, FREDERICK B. TAYLOR, VICTOR G. ALLENBURY, and HOMER ROBERTS—g. Symposium on pre- and postoperative care. Management of surgical patients and stomach cases, diabetes in surgery, traumatic and postoperative pneumonia, cardiac and renal complications, postoperative psychosis, allergy as related to abdominal surgery. Discussion and demonstration of cases

## PERALTA HOSPITAL

- J. L. LORR—g. Cholecystectomy  
 ERIC A. MAYNARD—g. Carcinoma of breast, radical resection  
 F. M. LORR and JOHN W. BARNETT—g. Porto caval anastomosis  
 CHARLES B. FOWLER—g. Orthopedic treatment of sporadic leishmaniasis, collection of upper extremity amputations in poliomyelitis  
 H. J. THOMPSON and J. LORR—g. 10. Electric desiccation in cutaneous malignancies  
 JOHN W. BARNETT—g. Vaginal plastic  
 T. FLOYD BELL—g. Pelvic tumor  
 T. C. LAWSON—g. Hernia, fascial repair  
 F. N. JACOBSON—g. Bladder surgery  
 FRED ALLENBURY—g. Pathological demonstration and exhibit  
 J. D. COLE—g. X-ray demonstration and exhibit

## COWELL MEMORIAL HOSPITAL

- HERBERT E. AND, ROBERT L. E. C. A. KOSKOFF and associates—g. Exhibit and discussion of latest advances in endocrinology, inspection of laboratories and hospital with special reference to the systematic medical care of university students. Discussion of laboratory technique with particular reference to anesthesia

## ALAMEDA SANATORIUM

- J. ORANGE—g. Hernioplasty under local anesthetic. Appendectomy  
 G. R. BURKE—g. Cholecystectomy  
 CLARENCE HALL—g. 30. Resection of stomach

## PROVIDENCE HOSPITAL

- O D HAMILTON—9 Intestinal anastomosis  
 J RADFORD FEARN—9 Vaginal hysterectomy under local anesthesia  
 A REIS—10 Cholecystectomy, new method  
 THEODORE M WELLER—10 Cesarean section  
 N AUSTIN CARY—11 Sacro iliac fusion  
 PHILIP J DICK—11 Posterior gastro-enterostomy  
 MICHAEL TORRANO—12 Herniotomy under local anesthesia.  
 S A JELTE—9 to 12 X-ray demonstration and discussion

## EAST OAKLAND HOSPITAL

- DON D WEAVER—9 Ulcer of the stomach  
 O R ETTER—9 Surgery in the diabetic patient, dry clinic.  
 R. G VAN NUYS—10 Dry clinic Visceroptosis and position of the viscera in healthy young adults, X-ray demonstration  
 BROOKS STEPHENS—10 30 Hallux valgus  
 CLAIR RASOR—10 30 Prolapse of uterus  
 ALEXANDER H. GRIFFITH—11 Carcinoma at the recto-sigmoidal juncture, Lahey technique

## SURGERY OF THE EYE, EAR, NOSE, AND THROAT

## CLINICS IN SAN FRANCISCO HOSPITALS—DAILY

## UNIVERSITY OF CALIFORNIA HOSPITAL

## Tuesday

- JOSEPH L MCCOOL, FREDERICK C CORDES, JOSEPH W CRAWFORD, C ALLEN DICKEY and DAVID O HARRINGTON—9 Ophthalmological operations  
 R. C MARTIN and FREDERICK C CORDES—9 Toti Mosher operation  
 WALLACE SMITH, LOUIS MORRISON and EDITH STOKER—9 Otolaryngological operations.

## Dry Clinics—2

- FREDERICK C CORDES Surgery of traumatic cataracts  
 J W CRAWFORD Tuberculosis of the eye.  
 C ALLEN DICKEY Surgery of the vertical muscles  
 DAVID HARRINGTON Contact glasses, practical demonstration.  
 R. C MARTIN and STERLING BUNNELL. Injuries and repair of the facial nerve

## Thursday

- JOSEPH L MCCOOL, FREDERICK C CORDES, JOSEPH W CRAWFORD, C ALLEN DICKEY and DAVID O HARRINGTON—9 Ophthalmological operations.  
 R C MARTIN and FREDERICK C CORDES—9 Toti Mosher operation  
 WALLACE SMITH, LOUIS MORRISON and EDITH STOKER—9 Otolaryngological operations.

## Dry Clinics—2

- JOHN SAUNDERS Regional anatomy of the mastoid and pathways of infection of the intracranium  
 HOWARD C NAFFIGER. Brain abscess arising from middle ear and mastoid infections  
 WALLACE SMITH Phlebitis and thrombosis following middle ear and mastoid infections.

## Friday—2

- FREDERICK C CORDES Surgery of complicated cataracts  
 J W CRAWFORD The eye in diabetes  
 C ALLEN DICKEY The value of orthoptic treatment.  
 DAVID HARRINGTON Tobacco amblyopia and its treatment.

## ST MARY'S HOSPITAL

## Thursday—2

- FRANCIS CONLAN, STANLEY BURNS and FRANK HAND Treatment of posterior sinusitis Blood dyscrasias in relation to the ear, nose and throat. Treatment of bilateral abductor paralysis  
 FRANK HAND Radical antrum

## SAN FRANCISCO HOSPITAL

## Tuesday—2

- WARREN D HORNER External incision, history, uses, technique and advantages  
 C. ALLEN DICKEY and J W CRAWFORD Safety procedures in cataract operations, akinesis, intra-orbital injections, lid sutures, pre-operative medication.  
 WARREN D HORNER, C ALLEN DICKEY and J W CRAWFORD The use of synthetic epinephrin bitartrate in ocular therapeutics  
 AUBREY RAWLINS Osteoma of the antrum, some curious foreign bodies in the lungs, cases of recovery from otitic meningitis, extensive osteomyelitis of the frontal bone  
 HARRINGTON B GRAHAM. Foreign bodies in the lungs, stenosis of the esophagus, cancer of the larynx  
 HARRINGTON B GRAHAM and J M WOLFSOHN Extensive abscess of the meninges  
 RAE ASHLEY Treatment of tuberculosis of the larynx

## HOSPITAL FOR CHILDREN

## Thursday—2

- GEORGE N HOSFORD and AVERY M HICKS Technique for the determination of the hydrogen ion concentration of tears The significance of pH of tears in ocular symptoms and treatment. Indications for and results of orthoptic training Relation of vertical imbalance of extra ocular muscles to gastric symptoms, posture, temperament and aptitude for school work and occupation. Congenital muscle palsy Motion picture demonstration of O'Connor technique for heterophoria and heterotropia

## Days to be Announced

- GEORGE N HOSFORD and AVERY M HICKS—9 Extraction of congenital cataract, muscle operations, O'Connor pinch shortening for simple exotropia, simple esotropia, vertical deviations, muscle transplants for external rectus palsy, superior rectus for paralysis of the superior oblique (Jackson's technique), Motais' operation for congenital ptosis, Toti Mosher operation for occlusion of nasolacrimal duct (with Drs Martin and Hosmer)

## STANFORD UNIVERSITY SCHOOL OF MEDICINE

## Wednesday—2

- FRANK RODIN Congenital and hereditary eye defects  
 AVERY HICKS Ocular torticollis  
 DOHRMANN FISCHER. Retinal detachment, methods and results



## MOUNT ZION HOSPITAL

## Tuesday

HENRY J. COHN, LEO DE LIZIOTT and JOSE SCARF—  
Tonsil operations, local and general anesthesia, dis-  
section, Shaker mastectomy

## Wednesday

HENRY J. COHN, LEO DE LIZIOTT and JOSE SCARF—  
Symposium on mastectomy  
GEORGE S. LACHINA—Treatment of cervical ulcer  
CHARLES V. LEE—Recently developed concepts in he-  
matology and bacteriology of value to the epithelial  
oncologist  
FRANK H. ROSE—Treatment of acute kidney disease  
O. Y. RICE—Pathological demonstration of various eye  
conditions

## Thursday

Staff—  
Major operations: Submaxillary resection, electro-  
coagulation of tubercular, sinus surgery

## Days to Be Announced

Dr. H. ROSE, and GEORGE S. LACHINA—  
Ophthalmological operations: Cataract, strabismus, plastic on  
eyelids

## SOUTHERN PACIFIC HOSPITAL

## Thursday

W. LEO F. SWART and JOSE C. W. LEE—Clinical and  
demonstration of cases

## CLINICS IN ALAMEDA COUNTY HOSPITALS—WEDNESDAY

## PROVIDENCE HOSPITAL

A. J. HOWELL—  
ROBERT O'CONNOR—  
GEORGE MCCLELLAN and ALBERT A. ALLEN—  
R. POLYMER BERAMETTER—  
ROY NELSON—  
WILLIS STEPHENS, JR.—  
FRANK BAXTER—  
MICHAEL H. SMITH—  
ALEXANDER GALLAGHER—  
W. A. MAGRADE—  
ALVIN P. WOOD—  
J. C. BRACAN—

## LEFFERTMAN GENERAL HOSPITAL

## Tuesday

A. E. SCHLAMMER and HERBERT H. PRICE—  
Tonsillectomies, adenoidectomies, general anesthesia  
HARVEY C. MAXWELL—  
Strabismus correction by O'Frawley  
tracheal resection and by JAMESON procedure

## Wednesday

A. E. SCHLAMMER—  
Tonsillectomies, local anesthesia  
nasal operations, local anesthesia

## Thursday

HARVEY C. MAXWELL—  
Eye operations: local anesthesia,  
cataract extraction, pterygium excision,  
strabismus correction

## Friday

A. E. SCHLAMMER, HERBERT H. PRICE and HARVEY C.  
MAXWELL—  
Sinus surgery, local anesthesia, exten-  
sive radical frontal ethmoidectomy, radical  
maxillary anastomosis, bronchography, nephrography

## ST. LUKE'S HOSPITAL

## Tuesday and Thursday

JOSEPH L. MCCOY, C. ALLEN DUNN, A. E. JACOBSON  
and CHARLES B. TAYLOR—  
Ophthalmological clinic

## VETERANS ADMINISTRATION

Staff—  
Bronchoscopic examinations

R. J. KOTTER—  
P. T. LEFFERTS—  
J. RAYMOND BROWN—  
WYOMING N. PARKMAN—

## Dry Clinic 2-4:30 p.m.

Staff—  
Discussion of operative procedures, demonstration  
of cases, lectures and medicine picture demonstration

## ALAMIDA SANATORIUM

B. M. STEPHENS—  
Cataract

## CHILDREN'S HOSPITAL

A. E. SCHLAMMER—  
Strabismus, operative treatment

# SURGERY, GYNECOLOGY AND OBSTETRICS

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## IRREGULAR SHEDDING AND IRREGULAR RIPENING OF THE ENDOMETRIUM

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FOR a number of years it has been increasingly difficult to account for the clinical history, as well as the physical and histological findings, of some of our patients suffering from functional uterine bleeding on the basis of the endometrial hyperplasia syndrome. As a result of this we have gradually come to the conclusion that there are other clinical entities with a corresponding histological picture in the endometrium which cause or are associated with metrorrhagia. Although these may be hormonal in origin they are quite distinct from hyperplasia of the endometrium. In this paper we shall outline the results of our study and indicate two entities, one of which has not hitherto been described, while the other has been recognized only in the German literature. These we feel probably account for from 20 to 30 per cent of the patients suffering from functional uterine hemorrhage, although many more observations will be necessary before their incidence and significance can be accurately known.

In 1850, Récamier designed the curette to remove "fungoid and granulation-like pieces of tissue" from the uterine cavity. In so doing, he provided a means of studying this tissue which changed completely the older concepts of endometrial disease. The study of tissue removed by curettage as well as of

uterine and ovarian specimens removed at operation, has enabled us from time to time to modify our ideas so as to bring them into consonance with the physiology of the ovary and the hypophysis as it has been unfolded.

Among the older writers, Rokitsansky, Scanzoni (1863), Pozzi, Olshausen (1875), Duncan (1879) and Rüge (1879) were largely instrumental in establishing inflammatory lesions of the endometrium as an explanation of the various types of abnormal endometrial bleeding, and the histological pictures which they found to be associated with them. Indeed, they were so successful that such descriptive terms as "endometritis diffusa fungosa," "endometritis polyposa cystica," "endometritis atrophicans," "endometritis interstitialis," and "endometritis glandularis" survived for years as the names for various histological findings in the normal and abnormal endometrium.

That the "hyperplastic endometritis" type, of these writers, was not due to an inflammatory lesion was first enunciated by Brenecke (1882) and corroborated in rapid succession by de Smet (1884), Schmal (1890), and Cullen (1900). These authors found that hyperplasia of the endometrium was a distinct entity in no way associated with inflammation of the mucosa. Doederlein (1896), Pfannenstiel, Bumm, and Menge supplied the bac-

teriological work which was necessary to prove that these tissues were free from bacterial invasion.

However it was not until 1907 when Hirschmann and Adler made their classical contribution upon the cyclical changes in the normal endometrium, that it became clear that many of the so called endometritides were not only normal but had no relation to bacterial invasion. Now we know that true endometritis of the chronic type is a somewhat rare condition. Schroeder (1912) followed with his brilliant investigations upon the relationship of the normal endometrial cycle to the ovarian cycle, and thus were founded our modern concepts concerning the normal variations.

Schroeder (1919) followed his work upon the normal endometrial and ovarian cycle by an investigation into the hyperplastic changes in the uterine mucosa. He was able to confirm the work of the earlier group of writers, that etiologically hyperplasia of the endometrium was not of an inflammatory nature and further described its essential histological features and correlated it with the occurrence of graafian follicle cysts in the ovary suggesting that it was due either to the persistence of the follicle or to the lack of corpus luteum formation. Burch, Williams, and Cunningham (1931) have supplied convincing evidence in their animal experiments that hyperplasia of the endometrium is the result of the unopposed effect of the graafian follicle hormone estrin upon the endometrium.

This concept has been so firmly established and is now so widely recognized that not only is the disease accurately diagnosed clinically and histologically but a large literature has grown up about the subject. It would not be an exaggeration to state that probably 85 per cent of the so called functional uterine bleeding has come to be classified as due to hyperplasia of the endometrium. It will be interesting some day to know whether or not history is repeating itself whether or not we are committing the same enthusiastic error of the gynecologists of 1850 and 1860, in classifying so many patients as suffering from hyperplasia of the endometrium, instead of

from unknown or poorly understood diseases. Novak makes the statement "histologic examination of the endometrium in cases of functional hemorrhage, almost always reveals the picture designated as hyperplasia of the endometrium."

As our knowledge concerning the hormonal physiology of the endometrium has unfolded, it has become increasingly evident that not only the normal menstrual bleeding but some other types of endometrial bleeding of a pathological nature have a background in hormonal relationships. Hyperplasia of the endometrium was the first described and is perhaps the best understood of these. This syndrome undoubtedly accounts for the largest group of patients suffering from uterine hemorrhage of the functional type. Briefly stated it is considered to be a manifestation of prolonged and unopposed effect of the graafian follicle hormone estrin upon the mucosa of the uterus. This effect is apparent in curettage specimens in the overgrowth of the various elements composing the endometrium, both glandular and stromal. But more particularly it is characterized by a complete absence of any of the evidences of secretion such as the presence of glycogen etc. which have come to be recognized as the effect of the corpus luteum hormone upon the endometrium. In other words, hyperplasia of the endometrium may be considered to be the outcome of hyperestrin or graafian follicle effect without the formation of a corpus luteum with its ripening and secretory influence. It is therefore distinctly an abnormality of the proliferative or follicular phase.

The purpose of this paper is to call attention to two metropathies which do not seem to belong to the large hyperplasia group, but which probably are of a similar nature in so far as they may be the result of ovarian or other glandular imbalance.

The first of these presents such characteristic clinical and pathological details as to warrant its being described as a disease entity. English speaking gynecologists seem to have completely ignored or overlooked it, as nothing is to be found in the English language on the subject. For this reason and also because it is encountered not infrequently it seems



Fig 1 Irregular shedding of endometrium a, Secretory gland showing low exhausted type of epithelium and partial collapse, b, shrunken stroma with elongated nuclei  $\times 85$

important to describe this condition in some detail

In contradistinction to hyperplasia, irregular or incomplete shedding of the endometrium is an aberration of the secretory or corpus luteum phase. This differentiation is made at the outset because it is the impression of the author that much confusion exists concerning the histological findings in the idiopathic or functional types of uterine bleeding.

In 1924, Pankow described 3 cases of menorrhagia in women whose previous menses had been quite normal, but who had experienced excessive and prolonged menorrhagia during the period just prior to admission to the clinic in Duesseldorf. Curettage of the uterus in these women produced an endometrium without an epithelial surface layer, but with compact, infiltrated stroma and collapsed glands. As an explanation, Pankow stated that he thought that these cases must represent a delayed regeneration phase. Although incomplete and quite inadequate, this is the first reference in the literature to this syndrome. Other writers who have had articles

on the subject are Robert Meyer and his pupils.

Kaufmann and Hoeck, in describing a large series of patients (147) suffering with various forms of endometrial bleeding, referred to one group of 6, which, from their descriptions of the clinical findings as well as the appearance of the endometrium, indicate that these patients were suffering from irregular shedding of the endometrium or a closely allied difficulty.

Bamecki, in 1928, described 32 cases of irregular shedding of the endometrium from a series of 465 curettage specimens (an incidence of 7 per cent). This well considered article gives the clinical and histological findings in detail.

In the past year we have had 11 patients from a series of 97 who have suffered from functional bleeding of the endometrium, who seem to fall into this category, an incidence of 10 per cent indicating that it is not a rare condition. Clinically, these patients covered an age range of from 23 to 50 years, the majority of the patients being between the ages of 23 and 40 years.

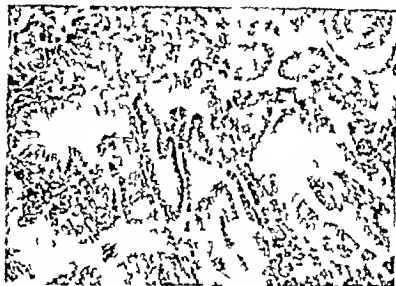


Fig. Irregular shedding of endometrium. Collapsed glands with low secretory epithelium & streaks partially necrotic stroma.  $\times 85$ .

These women all gave a history of having had normally regular menstrual periods until they came under observation because of a prolonged and profuse menses or of recurrent bleeding immediately following what was supposed to have been a normal menstrual period. The duration of the bleeding was from 10 to 43 days in the majority however from 8 to 14 days. Estrin determinations on the blood of 4 of these women showed an almost complete lack of this hormone. Likewise the prolactin titer in the blood stream was low. Unfortunately we have no adequate biological test for the corpus luteum hormone progesterin.

The genital organs as determined by inspection of the external genitalia, vagina, and cervix, as well as by bimanual palpation, were entirely normal. In addition no constitutional disease or other endocrine imbalance was encountered. Such causes of bleeding as abortion, polyp, myomata, endometritis, and disease of the adnexa were carefully ruled out.

The curettage material showed wide variation in the thickness of the mucosa and the size of the various pieces of endometrium. The material prepared by fixation in alcohol

formol and stained with hematoxylin and eosin, Papanheim's stain (for demonstration of plasma cells and possible infection) and with hematoxylin and Best's carmin (for determination of glycogen secretion) showed a definite and characteristic histological picture. The stroma is shrunken and composed of many deeply basophilic spindle-shaped nuclei. The spiral arterioles vary somewhat, but usually are dilated and engorged. Occasionally but particularly in those who have bled for some time there are thromboses of these vessels. In some cases there is extravasation of the blood elements into the stroma. The glands of the peripheral portions of the endometrium are collapsed to form bizarre shapes, many of them suggesting three, four and five pointed stars. The epithelium is obviously in the secretory or corpus luteum phase, as nuclei of the cells are discrete and located at the base of the cells, while the cytoplasm is clear though low and irregular in outline, suggesting prolonged activity. The Best's carmin stain further corroborates the secretory phase as many of the epithelial cells contain granules of glycogen which stain bright red with this medium. Other glands may show little or no secretory activity. But

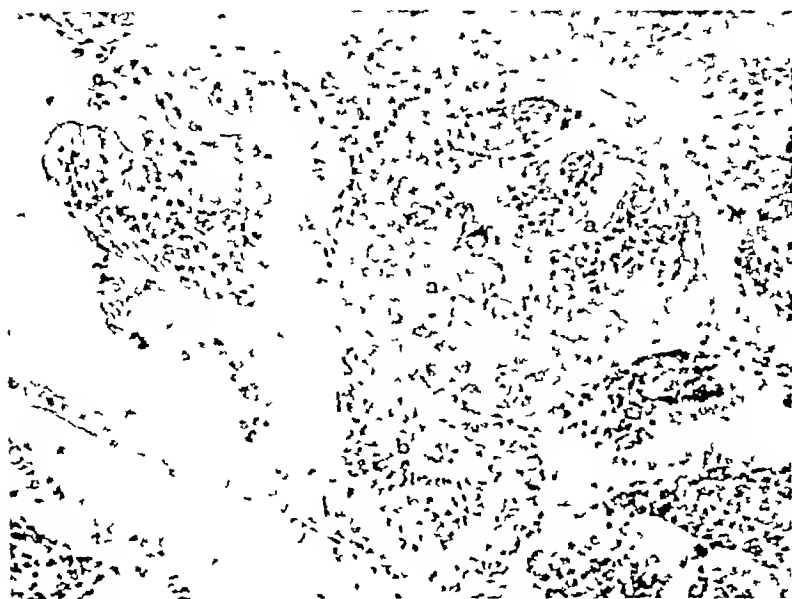


Fig 3 Irregular shedding of endometrium a, Collapsed "star shaped" glands with secretory epithelium, b shrunken inactive stroma  $\times 85$

for the most part, the impression gained by study of tissue from such a patient is that it is predominantly a secretory membrane. This should serve to distinguish it from hyperplasia which is just as markedly non-secretory, or proliferative in type.

The work of Bartelmez has shown that in normal menstruation the shedding of the spongiosa is a progressive phenomenon in the sense that there is focal shedding at a given time and that subsequently other foci bleed and shed in succession. Indeed, the duration of the menstrual period may be considered to be dependent upon the rapidity with which the various local processes succeed one another. In the light of this knowledge it would seem probable that in this type of menorrhagia we may be dealing with nothing more complicated than a very much prolonged menstrual period. This brings us to a consideration of the factors which might be responsible for such a physiological abnormality. As the corpus luteum is in the ascendancy during this phase of the cycle, the most logical explanation would seem to be connected with that body or remotely with the hypophysis. All the histological evidence

seems to point toward a prolonged and weak corpus luteum effect. In 2 patients in whom we were able to examine the ovaries, corpora lutea were found presenting evidence of degeneration in the form of fat droplets in many of the cells. However, there were substantial zones of lutein cells which had the appearance of being well preserved and probably actively secretory. It is to be regretted that more observations of ovarian tissue have not been possible, but the nature of the malady does not often offer the surgeon an adequate indication for laparotomy, and still less oophorectomy. Unfortunately, also, we have no reliable biological test for the corpus luteum hormone, progesterin, so that it is at the moment impracticable to demonstrate an alteration in the amount of the available hormone in these patients. For the time being, the explanation must remain theoretical. The possibility of a deficiency in the anterior lobe hormone has been thought of, and in a few of the patients under our observation the blood titer of this hormone has been demonstrated as low. However, this data is of academic interest until a great many more observations are possible, and mention is



Fig. 4. Irregular ripening of endometrium, two areas contrasting proliferation and secretory activity in the same endometrium at the same time. Both are from the functionals. The difference in reaction is marked in both glandular and stromal elements.  $\times 85$ .

made of it at this time purely as a matter of theoretical interest.

The history of the patient and the histological findings point emphatically to maldeciduation of the endometrium, with prolonged and exhausting secretory activity in the gland elements of those fragments of the spongiosa which remain attached to the basalis, while the trunks become broken and most often the cells have changed from the large round

nucleated forms to the spindle-shape which is characteristic of the proliferative phase of the cycle.

The treatment of this condition is simple. Our stage in our experience has sufficed with its removal of the remaining endometrium to cause prompt cessation of the bleeding. The women then resume their normal cycle. In only one patient have we twice encountered this condition. However it is to be expected



Fig 5 Irregular ripening of endometrium showing marked variation in response in different parts of the same tissue  $\times 85$

that with greater attention on the part of gynecologists to this syndrome, not only will it be more frequently recognized, but it will be found to recur in the same individuals

The second entity to which we wish to call attention differs from both the hyperplasia

and the irregular shedding groups, for these represent two different phases of ovarian activity the first, the graafian follicle phase and the latter, that of the corpus luteum, whereas, the one now to be considered represents a mixture of both proliferative and secre-





Fig. 6. Irregular opening of endometrium. Glands and stroma in proliferative phase & early secretory glands and stroma.  $\times 85$ .

tory phases. In our study of 100 patients suffering from functional bleeding of the endometrium, we encountered this mixed histological picture in 21: hyperplasia in 68 and irregular shedding in 1. Nine of the 21 patients were within 40 and 45 years of age; 3 were between 35 and 40; 7 were between 25 and 30; 1 was 15 years of age and 1, 55. Fifteen patients had given birth to one or more full term infants, none of which had been borne within a year of the time at which they presented themselves with metrorrhagia. Six had never been pregnant. Three were obese, and 1 had an enlarged thyroid gland with a normal basal metabolic rate. In none of the groups was there found any cause for the excessive bleeding such as malpositions or malplacements of the uterus, polyp of uterine or pelvic infection, myomata or malignancy. The tissues were prepared as described.

Histological examination revealed in these 21 cases an endometrium which in the peripheral zone showed considerable areas which were definitely non-secretory and others which were just as definitely secretory. The criteria which governed us in deciding between the proliferative and secretory phases were those enunciated by R. Schroeder and R. Meyer: the contour of the glands, the character of the lining glandular epithelium, whether or not

glycogen could be demonstrated in the glands, and the shape and size of the stroma cells.

In the endometrium of 5 of the patients, the predominance was in favor of the non-secretory type with here and there a few secretory glands scattered diffusely among them. These cases could obviously be regarded as early secretory endometria. In the 16 other patients, the endometrium showed a more patchy distribution as regards secretion and non-secretion. For instance an area in the vicinity of a spiral arteriole often shows many definitely secretory glands, occasionally with every evidence of well established secretory activity and frequently giving the impression of prolonged secretion because of their single layers of low clear epithelial cells with round pale-staining nuclei. Other areas show just as definite a proliferative phase, but with none of the criteria sufficiently developed to allow a diagnosis of hyperplasia. We have called this picture "irregular ripening" perhaps a better one would be irregular maturation of the endometrium. Certainly the impression gained from a study of the tissues is that of a patchy or irregular corpus luteum effect in an endometrium otherwise in the proliferative phase.

It is well recognized by histologists that the basal layer of glands adjacent to the myo-

metrium are almost completely unresponsive to the secretory stimulus of the ovary. They remain constantly in an inactive or proliferative status. For this reason, we have been most careful in our observations to be sure that we were dealing only with the more superficial layers of the endometrium, the functionalis. For similar reasons we were careful to rule out myomata and polypi, for in the vicinity of submucous or mural fibroid tumors, the endometrium is frequently refractory. The same may be said for the endometrial content of polypoid bodies. In addition, it has frequently been pointed out that in an otherwise secretory membrane an occasional gland may be observed which fails to react to secretory stimuli, maintaining throughout the cycle a proliferative type of epithelium. Various observers have ascribed this to persisting immaturity of the epithelium. In our study of the subject only areas in which a considerable number of glands were involved have been included in the category of irregular ripening.

Interestingly enough, 14 of the 21 patients presenting this histological picture commenced to bleed at approximately the middle of the intermenstrual period, at a time when one should expect that the hormones of both the granulosa cells and the lutein cells would be circulating in the blood stream. The difficulty in securing hormonological data in these patients lies in the fact that the diagnosis is not possible until the tissue is examined with the microscope. This, of course, is some time after curettage, so that there is no assurance that the picture presented is that which brought about the condition. It is quite probable, however, that the estrin titer is low. This is our impression, though we have not sufficient data at hand to make the statement positively. If it is demonstrated that this is a constant concomitant of the bleeding phase, it would correspond well with what we know in regard to hyperplasia of the endometrium and also with irregular shedding of the endometrium. Should we find a low estrin concentration in the blood as a usual feature of endometrial bleeding, whether normal or pathological, then we might conclude that the bleeding mechanism is independent of histo-

logical findings. Until more data are available, it may be wise to cling to the older point of view, that both blood loss and tissue change are linked to the same process and that each is in at least some degree an expression of the other. However, we are convinced that many women have a marked proliferative abnormality of the endometrium, with graafian follicle cysts in the ovary with no excessive blood loss, and we have seen 2 cases in which there was amenorrhea. The mechanism of endometrial blood loss is not understood and certainly the more we learn concerning it, the more we are impressed with the independence it may show of the factors controlling tissue change. Irregular ripening of the endometrium may possibly be explained by postulating an instability of the bleeding mechanism during the interval portion of the menstrual cycle. However, this bleeding is not that associated with the "mittel schmerz" but amounts to such a blood loss as to alarm the patient and take her to her physician for advice, and may, therefore, be considered as a definite metrorrhagia.

These patients, in a manner quite similar to that described for irregular shedding of the endometrium, have, in our experience, responded promptly to curettage and have not had a recurrence of the disease. We are at a loss to explain the non-recurrence because we feel that the disease has its origin in a quantitative imbalance of the ovarian hormones. This curettage should not remedy in all cases. It is felt that further experience and observation will reveal that this group of patients is as varied in its response to treatment as are those concerning whom more is known. The simplicity of treatment and the good prognosis in these diseases contrast sharply with some aspects of hyperplasia of the endometrium. However, they are of real interest and importance in the consideration of the ultimate causes of abnormal endometrial bleeding.

#### SUMMARY

A form of endometrial bleeding has been described probably due to glandular imbalance, most probably associated with the corpus luteum of the ovary, in which the woman fails to shed the surface spongiosa of

the endometrium normally and with which is associated excessive blood loss. This syndrome was first described clinically by Pankow who was succeeded by Robert Meyer and his pupils in further clarifying the histological details. A series of patients has been carefully studied and the clinical and pathological details confirmed together with suggestive data concerning possible hormonal relationships. In addition a second histological picture which we have named "irregular ripening" has been described together with the associated clinical facts which may or may not be an entity associated with excessive blood loss from the endometrium. Both have

been neglected by students of uterine bleeding, although in our experience they account for approximately one third of all functional bleeding. They are presented as separate syndromes although possibly related and with the full realization that the irregular ripening may be merely an early stage of the irregular shedding of the endometrium.

## REFERENCES

- BAWICKI, H. *Zentralbl f Gynaek* 92, 52-55  
KALMANN and HORN. *Zschr f Geburtsh*  
*Gynaek*, 1937 60 594
- 3 MEYER, R. *Handb d spec path Anat Hist*  
(Henske Lubarsch) 93, 7 1-5
- 4 PANKOW, O. *Monatschr f Geburtsh u Gynaek*  
92, 67-7

## FUNDUSECTOMY IN THE TREATMENT OF PEPTIC ULCER

## AN EXPERIMENTAL STUDY

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**S**URGICAL measures in the treatment of peptic ulcer have been directed into several rather definite channels first, the closure of perforations, second, the care of massive hemorrhage, third, the diversion of gastric contents around an obstructed pylorus, fourth, a rather broad and elastic group of procedures, of infinite variety and all of a plastic nature. Operations in the last category are designed to lower the gastric acidity by permitting an easier regurgitation of alkaline duodenal secretion into the stomach and effecting at the same time a removal of all or part of the ulcer bearing region of the stomach and duodenum. It is within this fourth group that so many unsatisfactory surgical experiences arise. The relief afforded patients with peptic ulcer by alkaline therapy continually urges the surgeon to devise an operation which will reduce gastric acidity alone without injuring the function of the pylorus.

Because surgical attempts to reduce gastric acidity by dilution of its secretion with intestinal alkalis through some operation that does away with the pylorus have not been of great success, the other logical step, as pointed out by Connell in 1929, is the removal of the acid secreting tissue. The problem connected with such a procedure is the question of how permanent the reduction might be in the face of the body's inherent capacity to hypertrophy the remaining glandular elements.

The fundus of the stomach having long been recognized as the site of acid secretion, Connell (1), in 1929, first suggested fundusectomy as a method of decreasing gastric acidity. In the same year, Deloyers and Johnson removed the fundus of dogs and found a consistent fall of gastric acidity both free and total at the tenth postoperative day. No additional studies were made by them at later dates. Connell (2), in 1931, reported his results from fundusectomies in dogs. He removed one-half of the greater curvature in a V shaped pattern,

taking both anterior and posterior gastric walls up to a finger's breadth from the lesser curvature. Aspiration studies showed a primary drop of both free and total acidity with a slow recovery of the total acidity alone. Meanwhile the gastric capacity had returned to normal. Sections taken later along the scar of the fundusectomy revealed no increase in parietal cells along the fundic glands. Fauley, Strauss, and Ivy, in 1932, published the results in a series of gastric resections performed on dogs in which approximately two-thirds of the stomach was removed in a procedure analogous to the Finsterer operation. This operation is essentially a resection of the pylorus, antrum, and varying heights of the fundus, closure of the duodenum, and anastomosis of the stomach to jejunum. A part of the gastric hiatus is closed with sutures in a manner to direct the food stream downward through the jejunum and to prevent retrograde filling of duodenum. X-ray studies showed return to normal capacity of the stomach in 2 months with maximum enlargement by 6 months. Well developed fundic glands having the normal number of parietal cells were demonstrated in sections from the reformed fundus. The levels of acidity after a temporary fall returned to normal in 3 to 5 months. The authors considered polyphagia to be the cause for the rapid dilatation of the stomach rugæ. Watson, in December, 1933, reported studies of gastric acidity after fundusectomy in dogs. He removed one-half to four-fifths of the fundus, leaving cardia, antrum, and lesser curvature intact. A definite reduction in both free and total acidity was noted immediately after operation. In analyses 15 to 18 weeks after operation the variations from the normal were very slight and occurred only in dogs from which four-fifths of the fundus had been removed.

As an aid to the removal of all the acid secreting area possible, we first devoted some



Fig. 1, left. Section through cardia of normal dog stomach looking toward the esophageal opening. Rich distribution of rugae on greater curvature. Compare with Figure 3.

Fig. 2. Section through cardia of stomach from which the fundus had been removed. Rugae are absent in antrum.

study to the location of the endocrine parietal cells in dogs. Miyagawa has reported the position of parietal cells in humans and in certain animals. He found they began two-fifths of

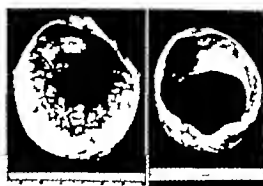


Fig. 3, left. A transverse block taken through the mid fundus of normal dog. Note smooth and parietal of lesser curvature and the numerous reduplication of mucous membrane over greater curvature.

Fig. 3B. Transverse block through the mid fundus of postoperative stomach. Rugae almost totally lacking.

the way along the lesser curvature toward the cardia and continued to the esophageal opening. He found as is well known that the greatest number were in the fundus. Nothing, however, had been said in regard to the comparative number of parietal cells in the lower and greater curvatures. In order to compare the two curvatures in this respect we removed the stomach from a normal dog, distended it with 10 per cent formalin, and suspended it in a jar of formalin. After having been properly fixed, rings were cut from the stomach at various levels through cardia, fundus, and antrum, and four blocks were taken from each ring, making the blocks correspond to the anterior and posterior walls of the stomach and saddles from both curvatures.

The distribution of parietal cells was found in our sections to extend well into the antrum, throughout which a few were always demonstrable almost anywhere. There were approximately the same number of parietal cells along a given gland in the lesser curvature as on the greater curvature. The number of glands per millimeter of mucosa was also equal. The superiority of the greater curvature as an acid secreting bed lies in the great reduplication of its mucous membrane by the rugae which are exceedingly well developed in the dog. (Figs 1A, 2A, 3A.) Numerous parietal cells were found along the fundic glands of the cardia. From these studies, it seemed apparent that



Fig. 3A, left. Transverse block from normal stomach through lower fundus looking toward the pylorus. Greater curvature rich in rugae which extend all into antrum.

Fig. 3B. Transverse block from stomach through lower fundus looking toward the pylorus. Fundus remains free of rugae.

in order to reduce gastric acidity by surgery it would be necessary to remove almost all the fundus and cardia leaving merely a slender tube from the esophageal opening to the antrum.

In January 1933 we began a series of very radical resections of the fundus in dogs attempting to leave only a tube from the esophagus to the antrum which would be made up chiefly of the *nagengasse* which in dogs measures some 4 to 5 centimeters in width. Such a tube would, of course, be free of rich acid secreting rugae.

#### EXPERIMENTS

Healthy dogs of nondescript breed weighing from 15 to 20 kilograms were selected. Three gastric analyses were done at intervals of 2 to 3 days on each dog. The test meal consisted of 100 grams of chopped beef and 250 cubic centimeters of water. Aspirations were made of fasting contents. In one dog the meal was given, and aspirations were made at 30, 60 and 90 minutes. This was followed by the intramuscular injection of 1 cubic centimeter of histamine hydrochloride and aspirations performed at intervals of 20 and 40 minutes. Titrations of specimens were carried out with one-tenth normal sodium hydroxide with Topfer's reagent and 1 per cent phenolphthalein as indicators for end points of free and total acids, respectively. After three satisfactory pre-operative gastric analyses were completed, the dogs were subjected to operation. They received 0.015 gram morphine sulphate by hypodermic injection 30 minutes before operation. They were anesthetized by cone-ether which was replaced by intratracheal insufflation of ether. The abdomen was shaved and skin prepared by alcohol 70 per cent, followed by oxycyanide of mercury in a solution of 1:2000. A linear, left, paramedian incision from costal margin to umbilicus was made. The stomach was isolated and the abdominal cavity protected with gauze. The blood supply along the greater curvature for the same distance as we expected to resect was doubly clamped, divided, and ligated with fine silk. The right gastro-epiploic artery was divided about 4 centimeters from the pylorus along the greater curvature. Small Payer clamps or

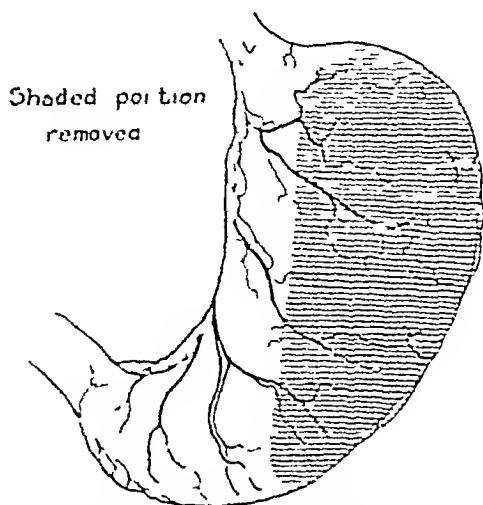


Fig. 4. Schematic drawing of dog's stomach. Shaded area indicates section removed at funduslectomy.

heavy Kocher hemostats were placed in pairs beginning usually about 4 centimeters from the pylorus and extending obliquely toward the lesser curvature. The points of the clamps were allowed to come within 3 centimeters of the lesser curvature. The stomach was then incised between the clamps. Before proceeding further along the lesser curvature, the medial clamp was removed, and the hiatus was closed. Pairs of clamps were then applied parallel to the lesser curvature, the medial clamp being placed always 3 centimeters from the lesser curvature. The stomach was divided between the clamps all the way up to the esophageal opening. The stomach incision was closed with a continuous atraumatic suture followed by another layer of interrupted silk mattress sutures inverting serosa to serosa. The abdominal incision was closed in four layers of silk. The shaded area of Figure 4 indicates the amount of fundus removed.

In the postoperative care the dogs were given 500 cubic centimeters of normal saline intravenously immediately following operation and this was repeated with added glucose for 3 days. At the end of this time the dogs were allowed to drink water and in 5 days, milk. After this they were gradually allowed larger and larger amounts of a soft solid diet. The feedings were made purposely small, and while the dogs ate well there was little of the

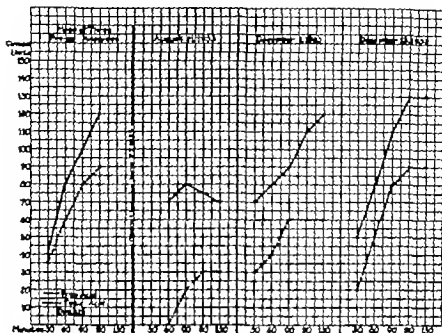


Fig. 5 Chart of analyses of expirations from Dog 5

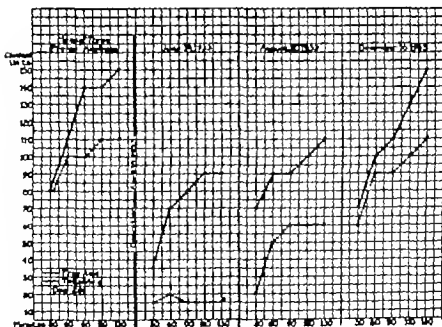


Fig. 6 Chart of analyses of expirations from Dog 101

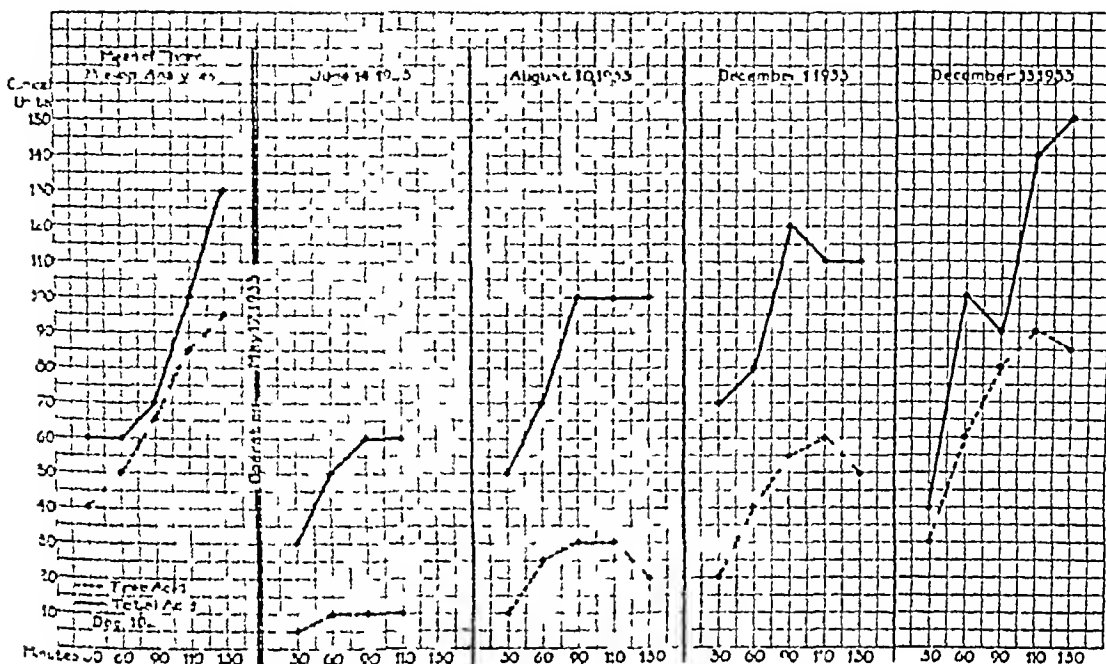


Fig 7 Chart of analyses of aspirations from Dog 10

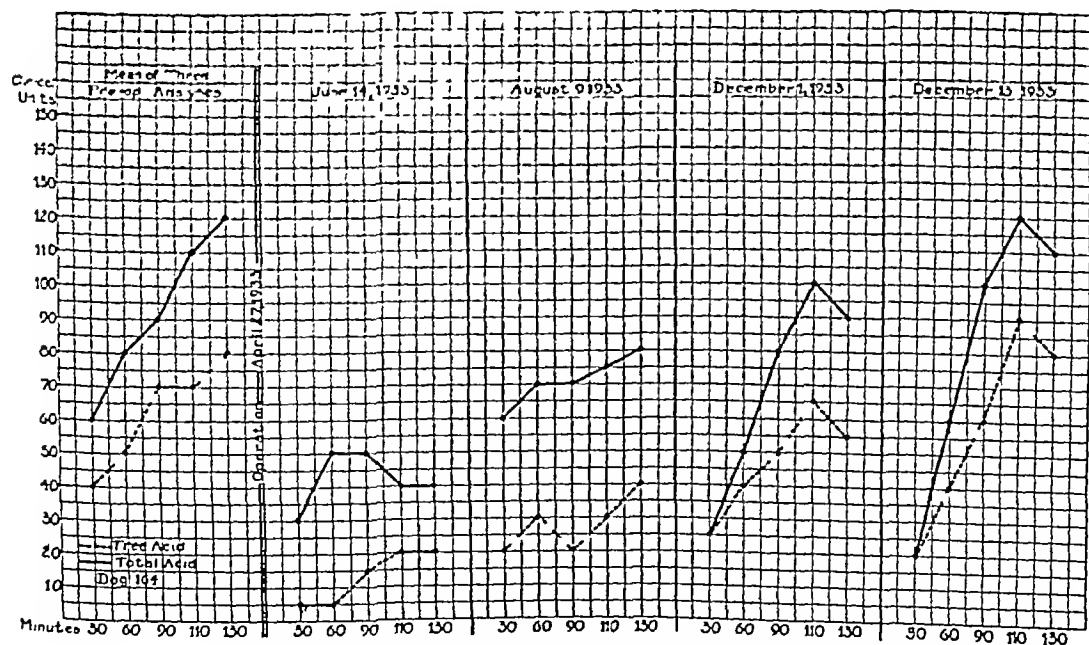


Fig 8 Chart of analyses of aspirations from Dog 164





Fig. 9. Normal stomach above. Resected stomachs below. Note approximate return to normal size and shape.

polyphagia described by Fauley, Strauss, and Ivy. For the first 2 weeks following operation there was occasional vomiting, but no signs of obstruction developed. The stools were normal. The dogs lost weight steadily for 1 month following operation, and then began to improve, regaining their weight and former vigor by the end of 4 months.

#### RESULTS

Gastric analyses exactly similar to the pre-operative test were performed 1 month after operation. The determinations consistently showed a substantial drop of both free and total acid. Three months after operation the levels began to ascend and continued to rise, reaching pre-operative levels 8 months after operation (Figs. 5, 6, 7, 8).

When the gastric acidity had reached pre-operative heights, the dogs were sacrificed. The stomachs were immediately removed, the pyloric lumen tied off, the stomach distended with 10 per cent formalin, and the esophageal opening tied. The stomachs were then suspended in a 10 per cent formalin bath in an effort to maintain their normal shape and outline during the period of fixation. Care was taken not to distend the stomachs too tightly, and one stomach was purposely only half filled

with formalin. After fixation, the stomachs were examined, and all were found to have regained a normal size and shape without strictures. Figure 9 is a group photograph of all the specimens in comparison with a normal stomach fixed in a similar manner. The stomachs were opened by guillotine section at various levels and photographs taken (Figs. 1B, 2B, 3B).

The *magenstrasse* was clearly demarcated from the rugae in the normal stomach as in Figures 1A, 2A, 3A, but in the stomachs from which the fundus had been removed, there were almost no rugae above a point 4 centimeters higher than the pylorus. The stomach walls above this point were smooth and resembled entirely the character of the normal *magenstrasse*. This was apparently not due to our distention for in the stomach half filled with formalin the same appearance was present. Evidently hypertrophy of the stomach does not extend to the production of new rugae at least within a year.

Microscopic sections of the lesser and greater curvatures were made at various levels. There was a generous distribution of acid reacting cells throughout, but this was most marked along the greater curvature. Histologically these cells were filled with secretory granules

and vacuoles suggesting that they were actively forming hydrochloric acid

#### SUMMARY

1 The literature on removal of the fundus of the stomach for the reduction of gastric acidity is reviewed

2 The gastric fundus was resected from 4 dogs leaving a tube about 5 centimeters in diameter from the esophageal opening to within 6 centimeters of the pylorus. This tube was made up chiefly of *nagerstrasse* smooth and free of ruga

3 Immediate postoperative drop of both free and total acidities was found, as compared to the pre-operative levels

4 There was a gradual return of the free and total acid reaching pre-operative levels by the end of 8 months

5 The stomach at necropsy showed hypertrophy to normal size and outline without reproduction of ruga

6 Microscopic examination of the post-operative stomachs showed a rich distribution of active acid bearing cells, especially along the greater curvature

#### CONCLUSIONS

The experimental findings agree with the clinical observation that the gastric acidity cannot be permanently lowered regardless of the amount of acid bearing tissue removed

Fundusctomy has little to offer as a means of permanently reducing gastric acidity and as a possible therapeutic measure in the control of peptic ulcer

#### BIBLIOGRAPHY

- 1 CONNELL, J. G. Fundusctomy, *Experimental Surg., Gynec. & Obst.*, 1931, 53, 750-752
- 2 Idem. Resection of fundus of stomach for peptic ulcer. *Ann. Surg.*, 1932, 95, 200-203
- 3 DELORME, J. and JONES, J. W. S. A. Recherches sur la topographie des régions elaboratrices de l'acide chlorhydrique dans l'estomac. *Presse med.*, 1929, 37, 570
- 4 FULFORD, G. B., STRAUSS, H. A., and IVY, A. C. Studies on effects of subtotal gastric resection in dogs. *Am. J. Surg.*, 1932, 17, 427-433
- 5 INSTITUTE, H. and CUNNINGHAM, F. Surgical treatment of duodenal ulcer. *Surg., Gynec. & Obst.*, 1931, 52, 1000-1114
- 6 MAYER, A. The exact distribution of the gastric glands in man and in several animals. *J. Anat.*, 1900, 55, 56-67
- 7 WATSON, J. R. The effect of experimental fundusctomy on the acidity of the gastric and duodenal content of the dog. *Proc. Staff Meet. Mayo Clin.*, 1933, 8, 735-737

## "PEPTIC ULCER AND THE ANXIETY COMPLEX"

THE FAILURE OF PHARMACOLOGICALLY SUSTAINED HYPERSECRETION AND HYPERMOTILITY OF THE STOMACH TO PRODUCE CHRONIC GASTRIC ULCER IN DOGS

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**D**URING recent years the belief that anxiety factors play an important rôle in the etiology of gastric and duodenal ulcer in man has been gaining favor (1, 14, 58, 60, 110, 116). We have seen, and the literature is replete with instances in which the recurrence of an ulcer has been associated with a period of sustained anxiety or mental distress.

This raises the question of what might possibly be the underlying perverted physiology concerned. It is well known that apprehension generally results in an inhibition of the motility and secretion of the stomach. In lower animals no one has ever recorded any other effect and one of us (A.C.I.) has to date failed by employing various types of conditioning procedures in the dog to produce an "anxiety" hypermotility of the stomach. In man we have been unable to find report of a ray examination in those rather rare instances in which severe epigastric pain occurs following acute mental distress in the absence of ascertainable organic lesions. Alvarez (3) has informed us of 3 patients who suffered severe epigastric pain following strong emotional stimulation and on whom he made X-ray studies. In both instances he observed five or six waves passing over the stomach which gave it the picture of a sock filled with billiard balls.

The studies of Todd (118) on medical students are more enlightening. He studied the stomachs of his first year students soon after they entered medical school and followed the behavior pattern of the stomachs of his students during the second year. These studies were continued for several years and have provided us with the only evidence we have of this nature. Among the observations pertinent to this discussion he found (a) through training or conditioning, the human stomach,

like that of the dog (66) may no longer be influenced by inhibitory psychic factors (b) when the "conditioned stomach" shows instability in response to mental distress, the instability takes the form of hypermotility. Todd has stated that "hyperactivity of the stomach is always present in the anxiety complex and in patients consciously or subconsciously nervous but not afraid."

Since we are quite certain from animal studies (37) that the splanchnic nerves are primarily concerned in the psychic inhibition of motility and because of the predominant motor effect of the vagus on gastric tone and motility it is logical to assume that the "anxiety hypermotility" just referred to is primarily vagal in origin. In this connection it should be pointed out that fear in the dog, according to Florey (44) results in pallor of the colon. Although no similar observations have been made on the gastric mucosa to our knowledge it is reasonable to assume that possibly the same type of reaction occurs in the gastric mucosa, because of the vasoconstrictor activity of the splanchnic nerves. This is mentioned because of the neurogenic or "neurotrophic" theory of the genesis of ulcer advanced by von Bergmann and his school and an increased vasoconstrictor tone of the vessels of the mucosa is more readily conceived than the much more vague term, "neurotrophic."

Up to the present time no one has determined whether or not gastric or duodenal ulcer may be produced in animals by exposure to an environment which produces a condition of emotional stress over long periods. It is difficult to maintain such an environment. In our laboratory an attempt has been made to accomplish this by placing cats and dogs in adjacent cages, but this was not successful because the animals soon become conditioned

to each other's presence. Monkeys soon become adjusted to new surroundings and are not continually aroused by conditions which at first disturb them. When they are placed in a room where dogs are present, they show signs of agitation for only a short time. Even the wildest of jungle animals soon become accustomed to the unnatural conditions of captivity and, according to those who are familiar with their habits, show no sign of emotional stress, and rarely develop "peptic ulcer."<sup>1</sup>

Probably the most likely hypothesis concerning the manner in which anxiety may act as a factor in the production of ulcer is that it affects the motility of the stomach in such a way as to cause pylorospasm, hypermotility, or intragastric hypertension. An associated retention may bring about a hypernormal acidity of the chyme, or a high acid continuous secretion during the interdigestive phase (38, 68, 69). Another hypothesis is that anxiety factors provoke a prolonged vasoconstrictor, or a "neurotrophic" disturbance.

Because of the difficulty of maintaining animals in surroundings capable of producing prolonged or frequently repeated emotional irritation, we resorted to the use of drugs in an attempt to reproduce experimentally the conditions mentioned under the first hypothesis. The drugs which we selected, because they might be presumed to cause increased motor activity or even spasm of the gastric musculature, and hypersecretion, were, respectively, pilocarpine and histamine.

Other investigators have used histamine in the study of experimental gastric lesions, but none has injected the drug as frequently throughout the twenty-four hour period and over as long a period of time as we thought desirable.

Delayed healing of artificial defects in the gastric mucosa of cats and dogs has been observed following the administration of large doses of histamine (25, 42, 87, 105). Acute lesions have also been produced in cats, rats, mice, rabbits, guinea pigs and dogs by a similar procedure (24, 25, 57, 94).

Acute ulcers have likewise been produced in guinea pigs and rabbits by the administra-

tion of large doses of pilocarpine (46, 85, 111, 116, 124).

If anxiety be a factor in the production of "peptic ulcer," it probably exerts its influence through the nervous system. In this connection, it should be pointed out that *acute* ulcers have been observed accompanying brain lesions in man and experimental animals (22, 29, 36, 53, 78, 85, 115), and following section of the vagus (42, 53, 79, 104, 112, 127) and splanchnic nerves (30, 35, 81), and celiac ganglionectomy (30, 50, 54, 76) in animals. Stimulation of the vagi, both electrically (79, 116) and by means of pilocarpine, as well as paralysis of these nerves by means of atropine (111) has also produced acute gastric lesions. Section of the vagi in the rabbit produces chronic gastric ulcers (67).

In the present study we have attempted to determine if chronic ulcers could be produced in the dog by

- 1 A sustained stimulation of the motor activity of the stomach
- 2 Maintenance of the secretory activity at a constantly high level
- 3 Continuous motor stimulation together with a high acid level

#### METHODS

The dogs studied were divided into three series and were injected ten times daily for periods up to 66 days. Those in the first group received histamine, those in the second group, pilocarpine, and those in the third group a combination of the two drugs.

The drugs were injected subcutaneously every 2 hours for 10 doses. The animals were then fed a standard meal consisting of 200 grams of Swift's "Pard" dog food, 2 slices of bread, 200 cubic centimeters of milk and 200 cubic centimeters of water, and then 4 hours later the injections were started again. Under this routine, which was repeated daily until the termination of the experiments, the animals were kept under the influence of the drugs for 20 hours a day, and during the remaining 4 hours the stomach contained food. Gastric analyses, throughout the 24 hour period, were made one to three times a week.

At the completion of the experiments, the animals were sacrificed and careful autopsies

<sup>1</sup>Dr. Noback, New York Zoological Gardens

were performed. Sections were made of the liver, kidneys, adrenals, and stomach.

**Series A** The 13 dogs in this series received pilocarpine. Most of them were maintained on 2.5 milligram doses for periods up to 37 days, but a few received larger doses. Three were started with 5 milligrams, but because of severe toxic manifestations, this was gradually reduced to 2.5 milligrams on the second day. Three of the dogs received 65 milligrams in 11 doses, 30 milligrams in 5 doses, and 195 milligrams in 27 doses, respectively. The weights of the dogs varied from 6.6 to 15.9 kilograms.

**Series B** The 11 dogs in this series received histamine. Dogs 1, 10 weighing from 7 to 13 kilograms, received 1 milligram of the drug every 2 hours for 63 to 66 days. Dog 11 weighing 5.7 kilograms was given a total of 132 milligrams of the drug in 55 hours, at the end of which time he was sacrificed.

**Series C** The 25 dogs in this series received a mixture of pilocarpine and histamine. They were maintained on 2 milligrams of each drug for periods up to 58 days. One dog received 3 milligrams of pilocarpine and 2 milligrams of histamine for 55 days, and 4 dogs received massive doses up to 300 milligrams of histamine and 500 milligrams of pilocarpine in 39 doses over about a 4 day period. The weight of the dogs varied from 6 to 19 kilograms.

## RESULTS

**Series A** There was great individual variation among animals of the same weight in their susceptibility to the actions of similar doses of the drug. The drug stimulated the secretion of a gastric juice of fairly high acidity and rich in pepsin. Six dogs that developed severe pilocarpine intoxication showed extensive mucosal hemorrhages throughout the stomach and intestines. No changes occurred in the esophagus. The 7 remaining dogs were etherized after 37 days and showed no changes in the gastro-intestinal tract except a slight injection of the duodenum in some cases. All of the dogs of this series showed normal liver, kidneys and adrenals upon microscopic study.

**Series B** The subcutaneous injection of histamine caused a copious secretion of a

gastric juice of high free acidity. Measurements of the volume and titrations of the gastric contents of the dogs in this series (using dimethyl-amino-azobenzol as an indicator) revealed that the response to histamine was just as strong at the end of the experiment as at the beginning. It is clear therefore, that by our procedure, we were able to subject the gastric and duodenal mucosa almost constantly to the action of highly acid juice.

Dog 5 died of "distemper" and bronchopneumonia after 32 days. No lesions were found in the gastro-intestinal tract. The 9 dogs receiving 2 milligrams of histamine every 2 hours were sacrificed with ether after periods ranging from 55 to 66 days. Although small acute erosions were found in the duodenal mucosa of 4 dogs, in no case was a chronic ulcer produced. All of these dogs showed a roughened, leathery pyloric mucosa, as described by Flood and Howes (43) and we also sometimes observed mammillations. Microscopic examination of the liver, kidney and adrenals of these animals revealed nothing abnormal.

Dog 11 was given large doses (63 milligrams) of the drug (a total of 132 milligrams) and was etherized after 55 hours. Multiple single and confluent, irregular ragged and hemorrhagic mucosal defects were found throughout the stomach, most numerous in the fundus. Hemorrhages into both adrenals were also observed.

**Series C** The injection of a mixture of pilocarpine and histamine stimulated the secretion of a gastric juice of high acidity and peptic activity. The fact that diarrhea and vomiting frequently occurred (as well as salivation and lacrimation) indicated that the pilocarpine was producing its typical motor effects.

Six of the 25 dogs died of "distemper." All of these 6 dogs showed mucosal hemorrhages throughout the stomach and intestines, and in 3 there were erosions. Seven animals died of drug intoxication because it was impossible to forestall the marked variations in susceptibility of different animals to pilocarpine. Autopsy revealed mucosal hemorrhages throughout the stomach and intestines in all of these, and hemorrhagic erosions in 5 dogs.

The 12 remaining dogs were etherized after periods ranging from 36 to 58 days. At autopsy, one dog presented a small erosion in the stomach, but no lesions were found in any of the other animals. The pyloric mucosa in some cases showed mammillations.

The liver, kidneys, and adrenals were normal in this group also.

#### EVALUATION

A combination of histamine and pilocarpine is said, by Vineberg and Babkin (121), to activate all the known cytological elements of the gastric mucosa, producing a secretion approximating the juice secreted as a result of normal stimuli. Frequent analyses of the gastric contents of our animals assured us that throughout the duration of the experiments we were obtaining a continued secretory response to the drugs injected. It is evident, therefore, that the mucosa of the stomach and duodenum was almost continuously exposed to the action of highly acid gastric juice. The diarrhea observed in the dogs receiving pilocarpine indicated that the motor effects continued to be obtained throughout the period.

It is interesting to observe that the gastric glands resisted fatigue even after repeated stimulation and practically constant activity for periods up to 66 days. The response to the drugs was as active at the end of the experiments as at the beginning. This is in agreement with the observations of other investigators (11, 62, 117).

During the course of our experiments we have produced a markedly increased motor activity of the stomach and duodenum, and have caused the mucosa of these organs to be subjected to a prolonged and unusual exposure to acid gastric juice. We have, therefore, reproduced experimentally two of the conditions which, by theory, may result from "sustained anxiety" and have maintained these conditions for relatively long periods of time, but, a chronic "peptic" ulcer did not develop. It seems clear, therefore, that neither the continuous action of acid-pepsin, nor the continuous motor hyperactivity induced by pilocarpine can produce chronic ulcer in dogs. These two factors when acting together are likewise incapable of producing chronic ulcer.

It is obvious that some other factor is necessary for the production of chronic gastric and duodenal ulcer, at least, in the dog.

Many clinicians have considered that the digestive action of gastric juice is the prime factor in the etiology of chronic "peptic" ulcer (4, 86, 97). Others have maintained that the rôle of acid-pepsin is insignificant (3). Although we have demonstrated that the acid-pepsin when acting alone or together with a hypermotility factor as produced by pilocarpine cannot produce chronic ulcer, it appears to us that both clinical and experimental evidence is best interpreted as indicating that the acid factor plays some part (chemical irritation) in maintaining the chronicity and in some instances the rapid extension of such a lesion (4, 26, 34, 40, 47, 60, 69, 75, 83, 86, 92, 93, 95, 97, 98, 102, 106, 115, 122).

It should be pointed out that our dogs were fed a "smooth," ground diet. This is mentioned because unhygienic eating habits, e.g. improper mastication of meat and raw vegetables, consumption of much alcohol, hot and cold fluids, etc., are frequently associated with the "anxiety complex" in patients. A "rough food" has been shown to be a "chronicity factor" in ulcer (69).

The drugs, in so far as it is known, do not have a vasoconstrictor action, and possibly do not have a "neurotrophic" action in the sense that the latter term is generally used. These are the only two factors other than those discussed above which are thought to be directly concerned in the suggested "anxiety-ulcer" relationship.

#### CONCLUSIONS

1. We have been unable to produce chronic ulcers in dogs by exposing the mucosa of the stomach and duodenum for long periods of time to the constant activity of a gastric juice rich in acid and pepsin. The acid factor, acting together with hypermotility as produced by pilocarpine, likewise does not produce chronic lesions. Under these latter conditions, however, acute lesions of the gastric mucosa are very common. This indicates that some other factor is necessary for the production of chronic ulcer in the dog.

\* The gastric glands show no signs of fatigue even after practically continuous secretion for periods up to 66 days.

## REFERENCES

- AL. ARIZ, W. C. Light from the laboratory and the clinic on the causes of peptic ulcer. *Ann J Surg* 912, 8 207.
- Idem. Personal communication.
3. ARIZ, A., and JOSEPH, F. La pathologie chronique de l'ulcère gastro-duodénale en face de l'expérimentation. *Bouillon sécl* 930-193 667.
4. ARIZ, P. W. and KARELITZ, S. Peptic ulcer of Meckel's diverticulum and duodenum. *Ann Surg* 930, 9 573.
5. ARIZ. Quoted by Grogg.
6. BARNES, B. P. The acidity of the gastric juice. *Ann J Surg* 920, 7 498.
7. Idem. The value of histamine as a test of gastric secretion from a physiological point of view. *Canadian M. Ass. J.* 930, 23 268.
8. BASSO, G. L'ulcera che si fa protezione dell'ulcera duodenale viene esercitata dalla deviazione del contenuto gastrico. *Arch Ital di chir* 934, 330.
9. BERNARDI, N. V. Produzione sperimentale di ulcera gastrica. *Arch Ital di chir* 934, 9 90.
10. BIRD, B. N. and JOSEPH, J. W. Biliary and hepatic factors in peptic ulcers, an experimental study. *Arch Surg* 930, 90 907.
11. BIRSON, G. RICHMOND, M. F. and HAWK, P. B. Gastrointestinal studies III. Studies on water drinking (XXI). *J Biol Chem* 914, 9 545.
12. BIRSON, G. S. Effect of pilocarpine and histamine on gastric secretion. Unpublished data.
13. BIRSON, G. von. Das Spontaneous Ulcer pepticum Menschen und Wachschr. 935, 60 69.
14. Idem. Ulcus duodeni und gastrici Nervensystem. *Berl Klin Wochenschr* 935, 30 374.
15. BIRT, C. H. and McILROY, E. W. Histamine. *Physiol Rev* 935 377.
16. BIRCKEL, A. Beobachtungen an Hunden mit Exstirpation Duodeni. *Berl Klin Wochenschr* 909, 45 (III) 202.
17. BLACKLY, A. P. L. and WILLIAMS, J. F. The influence of histamine and pilocarpine on the human gastric secretion. *Brit J Exper Path* 935, 14 349.
18. BOLEMA, J. L. and MA, N. S. C. Chronic duodenal ulcer is associated with leak fistulas on certain days. *Arch P. th* 937 4 49.
19. BOLOV, C. Further observations on the pathology of gastric ulcer. *Proc Roy Soc Lond* 909, 83 35.
20. Idem. The part played by the acid of the gastric juice in the pathological processes of gastric ulcer. *J Path & Bacteriol* 935, 20 33.
21. BOWEN, M. Quoted by Grogg.
22. BOWEN, M. Quoted by Grogg.
23. B. SCHNEIDER, F. Magen- und Duodenal- und peptische Geschwüre. *Klin Wochenschr* 909, 9 (I).
24. B. SCHNEIDER, F. SCHNEIDER, P. and MOULIN, P. J. Ueber experimentell-energetisch akute peptische Geschwüre des Rattenmagenes. *Berl path Anat* 1934-930, 8 30.
25. BERNARDI, D. LA CANY, H. Zur Pathologie und Chirurgie der peptischen Geschwüre des Magens-Duodenals. *Deutsche Zeitschr f Chir* 930, 30 31.
26. BUTCHER, J. L. Ulcers of the gastro intestinal tract. 16th practical reference to gastro-intestinal ulcers. Papers from the Mayo Foundation and the Medical School of the University of Minnesota. Vol. 1, p. 57 Philadelphia W. B. Saunders Co 913-1930.
27. CARLSON, H. Hunger in Health and Disease. Chicago, 9 6.
28. CARRISON, HARVEY VI. Concerning possible parasympathetic control in the duodenum. *Proc Nat Acad Sci* 935, 7 53.
29. Idem. Peptic ulcer and the duodenum. *Surg Gynec & Obst* 935, 55.
30. DALLA VEDOVA, R. Ricerche sperimentali sulla patogenesi dell'ulcera gastrica. *Polonia* 909, 6 53 (Suppl).
31. DE TAKATS, G. and MARY, F. C. The effect on the jejunal mucosa of transplantation to the lower curvature of the stomach. *Ann Surg* 937 85 668.
32. DRASTREIT, L. R. Contributions to the physiology of the stomach. XXXVIII. Gastric juice in duodenal and gastric ulcers. *J Am M. Ass* 917 68 330.
33. Idem. Ulcers adhaes of Meckel's diverticulum. *J Am M. Ass* 1913, 30.
34. DRASTREIT, L. R. and VANDER, A. M. Gastric ulcer studies. The resistance of various tissues to gastric digestion. *Arch Surg* 922, 8 797.
35. DUKA, Y. L. The tropic element in the origin of peptic ulcer. *Surg Gynec & Obst*, 915, 300.
36. EASLEY, W. Experimentelle Untersuchungen über das Zustandekommen von Blinddarctum in der Magen-Duodenal-Region. *Arch f exper Path Pharmacol* 874, 83.
37. ELMAN, R. Spontaneous peptic ulcers of the duodenum following the total loss of pancreatic juice. *J Clin Invest* 935, 10 87.
38. ELMAN, R. and ECKERT, C. T. Neutralization of gastric acidity following pyloric closure. *Proc Soc Exper Biol & Med* 935, 30 343.
39. ELMAN, R. and HARTMAN, A. F. Spontaneous peptic ulcers of duodenum after continued loss of total pancreatic juice. *Arch Surg* 935, 3 1039.
40. ENALTO, J. Ulcus pylori nach Gastroenterostomie. *Mitt d Grenzgeb d Med Chir* 915, 35 5.
41. FAULTER, G. B. and IFT, A. C. Experimental gastric ulcer. The effect of the consistency of the diet on healing. *Arch Int Med* 930, 46 524.
42. FINZI, O. Ueber Veranderungen der Magen-Duodenal-Region bei Tieren nach Nebenaugenoperation und neuer experimentell erzeugte Magengeschwüre. *Arch f path Anat Physiol*, 935, 114 115.
43. FLOOD, C. A. and HOWES, E. L. Experimental study of the effect of histamine on the healing of gastric defects-artificial gastric ulcer. *Surg Gynec & Obst* 935, 58 50.
44. FLOREY, J. *Physiol* 930, 48 73.
45. FRIEDMAN, J. FRIEDMAN, M. and MONTAGNA, S. The effect of acids and other substances in the production of acute gastric ulcers. *J Am Gastroenterol Ass* 934, 35 327. *J Exper Med* 913, 37 303.
46. FRIEDMAN, G. A. The experimental production of ulcers, erosions, and acute ulcers in rabbits by repeated injections of pilocarpine and adrenaline. *J Med Research*, 918, 58 449.

47. FRIEDMAN, J C, and HAMBURGER, W W Experimental chronic gastric ulcer J Am M Ass, 1914, 63 380.
48. GALLAGHER, W J Acute traumatic ulcers of the small intestine Arch Surg, 1927, 15 689.
49. GALLAGHER, W J, and PALMER, W L Experimental jejunal ulcer relative importance of mechanical and chemical factors Proc Soc Exper Biol & Med, 1933, 30 405.
50. GIBELLI, D C Contributo critico sperimentale all' etiologia dell' ulcera gastrica in rapporto coi traumi Arch internat d chir, 1908 4 127.
51. GILMAN, A., and CONWELL, G K Effect of histamine on the secretion of gastric pepsin Proc Soc Exper Biol & Med, 1930, 23 104.
52. Idem. The effect of histamine upon the secretion of gastric pepsin Am J Physiol, 1931, 97 124.
53. GREGGIO, L Des ulcères gastro-duodénaux Arch de méd expér et d' anat path, 1917, 27 533.
54. GUNDELINER, E Klinische und experimentelle Untersuchungen ueber den Einfluss des Nervensystems bei der Entstehung des runden Magengeschwüers Mitt a d Grenzgeb d Med u Chir, 1918, 30 180.
55. GUNDERMAN, W Production expérimentale d'ulcères gastriques et duodénaux, contribution à l'étude d'une fonction pathologique du foie J de chir, 1914, 12 635.
56. HANKE, H Zur Pathogenese der experimentellen, akuten und erosiven Gastritis infolge parenteraler Zufuhr bestimmter pharmaca (Morphin, Pilocarpin, Caffein) Klin Wchnschr 1933, 12 1524.
57. HARDE, E Lésions gastriques des souris après injections répétées d'histamine Compt rend Soc Biol, 1932, 109 1326.
58. HAUSER, G Die peptischen Schädigungen des Magens des Duodenum und der Speiseröhre und das peptische postoperative Jejunalgeschwür Vol 1 Henke, F and Lubarsch, O Handbuch der speziellen pathologischen Anatomie und Histologie. Berlin Julius Springer, 1 1026.
59. HELMER, O M FOLTS P J and ZERFAS L G Gastro intestinal studies I J Clin Invest., 1932, 11 1129.
60. HOLT, G Versuche ueber die Selbstverdauung des Darmes im Magen Mitt. a d Grenzgeb d Med u Chir, 1910, 21 143.
61. HUGHSON, W Relation of the pylorus to duration of experimental gastric ulcer Arch Surg, 1927, 15 66.
62. IVY, A C Contributions to the physiology of the stomach. XLVIII Studies in water drinking Am J Physiol, 1918, 46 420.
63. Idem Contributions to the physiology of the stomach LII Studies in gastric ulcer Arch. Int Med 1920, 25 6.
64. Idem Studies on gastric and duodenal ulcer J Am M Ass, 1920, 75 1540.
65. Idem The etiology of gastric and duodenal ulcer Nebraska State M J, 1929, 14 137.
66. Idem Bull New York Acad Med In press.
67. IVY, A C, and BEAZELL, J Production of chronic gastric ulcers in rabbits by subdiaphragmatic vagotomy In press.
68. IVY, A C DROFGMUELLER, E H, and MEYER, J L Effect of experimental pyloric stenosis on gastric secretion. Arch Int Med, 1927, 40 434.
69. IVY, A C, and FAULEY, G B Factors concerned in determining the chronicity of ulcers in the stomach and upper intestine. Am J Surg, 1931, 11 531.
70. IVY, A C, and OYAMA, Y Studies on the secretion of the pars pylorica gastr. Am J Physiol, 1921, 57 51.
71. JONA, J L An experimental study of duodenal ulcer M J Australia, 1918, 1 165.
72. Idem A further contribution to the experimental study of duodenal ulcer M J Australia, 1919, 1 316.
73. Idem Experimental study of duodenal ulcer Physiol Abstr, 1919, 4 412.
74. KALL, H Ueber den Einfluss des Pilocarpins auf die Tätigkeit des menschlichen Magens Arch f Verdauungskr 1924, 32-33 219.
75. KAPANOW, R The experimental production of duodenal ulcer by exclusion of bile from the intestine Ann Surg, 1920, 83 614.
76. KAWAMURA, K Zur Frage der Verdauung lebenden Gewebes im Magen, zugleich ein Beitrag zur Pathogenese des runden Magengeschwüers Mitt. a d Grenzgeb d Med u Chir, 1913, 26 379.
77. KÄHNER, J K W Ueber die Ursache des runden Magengeschwüers Mitt a d Grenzgeb d Med u Chir, 1914, 27 679.
78. KELLER, A D HARE, W K, and D'ARMOUR, M C Ulceration in the digestive tract following experimental lesions in brain stem Proc Soc Exper Biol & Med, 1933, 30 772.
79. KERRICH, J Künstliche Erzeugung von chronischen Magengeschwüeren mittels Längsrisse am Magenvagus Wien klin Wchnschr, 1921, 34 118.
80. KIM M S, and IVY, A C The prevention of experimental duodenal ulcer by feeding neutral gastric mucin J Am M Ass, 1931, 97 1511.
81. KOENNECKE, W Experimentelle Untersuchungen ueber die Bedeutung des Pylorusmagens fuer die Ulcusergenese Arch f klin Chir, 1922, 120 537, Zentralbl f Chir, 1923, 50 276.
82. Idem Ulcusergenese und Gastroenterostomie Zentralbl f Chir, 1926, 53 1866.
83. LANGENSKJÖLD, F Ueber die Widerstandsfähigkeit einiger lebender Gewebe gegen die Einwirkung eiweisspaltender Enzyme Skandinav. Arch f Physiol, 1914, 31 1.
84. LATZEL, R Recherches expérimentales sur l'étiologie de l'ulcère de l'estomac et conséquences théoriques sur la pathogenèse de l'ulcère de l'estomac et du duodénum J de chir, 1913, 11 788.
85. LIGHT, R. U., BISHOP, C C, and KENDALL, L G The production of gastric lesions in rabbits by injection of small amounts of pilocarpine into the cerebrospinal fluid J Pharmacol & Exper Therap, 1932, 45 227.
86. LINDAU, A, and WULF, H The peptic genesis of gastric and duodenal ulcer Surg, Gynec & Obst., 1931, 53 621.
87. LITTHAUER, M Recherches expérimentales sur la pathogenèse de l'ulcère rond stomacal J de chir, 1909, 2 424.
88. Idem Experimentelle Untersuchungen zur Pathogenese des runden Magengeschwüers Arch. f path Anat. u. Physiol., 1909, 195 317.
89. LORENZI Quoted by Greggio.
90. MANN, F C The effect on the jejunal mucosa of exposure to the gastric juice. J Med Research, 1916-1917, 35 289.
91. Idem. The experimentally produced peptic ulcer Am J Surg, 1929, 7 453.
92. MANN, F C, and BOLLMAN, J L Experimentally produced peptic ulcers J Am M Ass, 1932, 99 1576.



- 93 MARR, F. C., and WILLIAMSON, C. R. The experimental production of peptic ulcer. *Ann. Surg.* 1913, 77, 409.
- 94 MATSUKURA, A. Zur experimentellen erzeugung des Magengeschwüres durch Histamine. *Klin. Wochenschr.* 1913, 9, 2265.
- 95 MATTHEWS, M. Untersuchungen über die Pathogenese des Ulcus rotundus ventriculi und über den Einfluss von Verdauungsorganen und lebendes und todes Gewebe. *Beitr. path. Anat. u. allg. Path.* 1893, 1, 300.
- 96 MATTHEWS, W. B. Production of intestinal ulcers by active gastric juice. *Proc. Soc. Exper. Biol. & Med.* 1913, 12, 960.
- 97 MATTHEWS, W. B., and DRASTETZ, L. R. The etiology of gastric and duodenal ulcer. *Surg. Gynec. & Obst.* 1912, 11, 265.
- 98 McCARTY, J. C. Experimental peptic ulcer. *Arch. Surg.* 1910, 9, 600.
- 99 McLELLAN, P. T. Experimental production of gastric ulcer. *Proc. Soc. Exper. Biol. & Med.* 1917-1918, 1, 363.
- 100 MOSTOV, C. B. Observations on peptic ulcer. I. A method of producing chronic gastric ulcer; a consideration of etiology. *Ann. Surg.* 1917, 65, 307.
- 101 Idem. Observations on peptic ulcer. IV. Patch transplants of jejunum in the stomach. *Ann. Surg.* 1917, 65, 379.
- 102 Idem. Observations on peptic ulcer. V. Findings in experimentally produced peptic ulcer: etiologic and therapeutic considerations. *Ann. Surg.* 1918, 67, 401.
- 103 NIKOLICH, H. LIMA, J., and VINCIGUERRA, F. Studies on extirpation. I. The fate of organs implanted into the duodenum. *Am. J. Physiol.* 1916, 70.
- 104 OBRIST, W. Gastric ulcers in rabbits following resection of the pneumogastric nerves below the diaphragm. *J. Exper. Med.* 1906, 5, 15.
- 105 O'SHEA, J. L. Etiology of peptic ulcer. *Lancet*, 1913, 80, 177.
- 106 PALMER, W. L. The value of acid neutralization in the treatment of gastric and duodenal ulcers. *Arch. Int. Med.* 1913, 16, 65.
- 107 POLLARD, W. S. Stimulation of gastric peptic by histamine. *J. Clin. Invest.* 1913, 4, 410.
- 108 POLLARD, W. S., and BLOOMFIELD, A. L. Quantitative measurements of peptic in gastric juice before and after histamine stimulation. *J. Clin. Invest.* 1914, 1, 57.
- 109 Idem. Diagnostic value of determinations of peptic in gastric juice. *J. Clin. Invest.* 1916, 6, 67.
- 110 REINERT, E. VON, and FÖRST, H. Die Pathogenese des peptischen Geschwüres des Magens und des oberen Darmabschnitts. *Neu-deutsche Chirurgie* Vol. 4. Stuttgart, F. Enke, 1918.
- 111 REINERT, M. E. The experimental production of acute toxic ulcer of the stomach. *Uch. Prou. M. Bull.* 1900-1901, 9, 33, 65.
- 112 RITTA, S. Contributo alla patogenesi dell' ulcera gastrica. *Gazz. d. med.* 1900, 11, 390.
- 113 RIVIERE, M. Leçons sur la physiologie de la digestion. Vol. 2. Florence, H. Lechevalier, 1897.
- 114 SCHWAB, Problem d. gastr. 1914, 4. Quoted by Babkin.
- 115 SCHWAB, I. S. Experimentelle Magen-duodenalulceration durch Schwefelsäure nach Pawlow. *Zentralbl. f. Chir.* 1917, 54, 115.
- 116 STARKER, E. Experimentelle Untersuchungen zur Frage der nervösen Entstehung des Ulcus ventriculi. *Arch. f. klin. Chir.* 1914, 371.
- 117 STRONACH, J. P. Der Einfluss des Histamins auf die Magensekretion beim Kanarienvogel nach lokaler Anwendung. *Skandin. Arch. f. Physiol.* 1913, 65, 9.
- 118 TONE. Behavior Patterns of the Alimentary Tract. Baltimore, 1910.
- 119 TROVATZKY. Dissertation, St. Petersburg, 1891. Quoted by Babkin.
- 120 VINCIGUERRA, A. M. The activation of different elements of the gastric secretion by variation of vagal stimulation. *Am. J. Physiol.* 1913, 66, 953.
- 121 VINCIGUERRA, A. M., and BLANK, B. P. Histamine and pepsinogen in relation to the gastric secretion. *Am. J. Physiol.* 1913, 67, 60.
- 122 WITZ, S. H. A case of peptic ulcer in the jejunum of dog following gastro-enterostomy, with review of the cases reported in men. *Bull. Johns Hopkins Hosp.* 1901, 14, 91.
- 123 WEISS, A. G., and GORDON, S. Sur une méthode permettant d'obtenir des ulcères gastro-duodénaux expérimentaux. *Compt. rend. Soc. de Méd.* 1913, 93, 43.
- 124 WESTPHAL, K. Untersuchungen zur Frage der nervösen Entstehung peptischer Ulcera. *Deutsche Arch. f. klin. Med.* 1914, 14, 117.
- 125 WESTPHAL, K., and KATZKE, G. Das secretische Ulcus duodeni. *Mitt. d. Grenzgeb. d. Med. Chir.* 9, 3, 26, 30.
- 126 KROVITZ, G. Contributo sperimentale alla patogenesi dell' ulcera rotunda dello stomaco. *Rivista med.* 1906, 11, 1045.
- 127 Idem. Experimenteller Beitrag zur Pathogenese des Ulcus rotundus des Magens. *Arch. f. klin. Chir.* 9, 9, 66.
- 128 ZIMMER. Verhandl. Gesellschaft Russ. Ärzte St. Petersburg, 1900. Quoted by Babkin.

## THE ROENTGENKYMOMOGRAPH AS A NEW AID IN THE DIAGNOSIS OF ADHESIVE PERICARDITIS

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THE roentgenkymograph is an instrument which records on an X-ray film, the amplitude of excursion of the heart borders during one or more cardiac cycles as predetermined by suitable adjustment of the instrument. The X-ray beam passes first through the patient and then through narrow horizontal slits in a stationary lead grid. Only the parts of the X-ray beam that pass through the narrow slits reach the recording medium (X-ray film). The film is kept in motion at a uniform rate of speed, and in a direction perpendicular to the slits, throughout the exposure. The exposure should be long enough to include one full cardiac cycle. The thin "pencil of light" that passes through the slit is modulated by the movement of the heart border and picked up in the form of a curve by the moving film. The differences in amplitude and timing of the contractions of the ventricles, atria, and great vessels are shown in the curves which represent the several portions of the cardiac silhouette.

Obviously the diagnostic value of the roentgenkymogram will depend upon the regularity with which changes from the normal can be shown in cardiac disease of known type. This will naturally require the accumulation and analysis of a considerable amount of data on the specific forms of cardiac disease. It will undoubtedly be found that certain types of cardiac disease will yield results of more diagnostic value than others. A case of adhesive pericarditis examined by the author gave striking results. The roentgenkymograms of the patient appeared to be susceptible of but one interpretation. The results obtained on this patient would appear to be of considerable importance especially to cardiologists and cardiac surgeons. As the method is relatively new and little known in this country, the roentgenkymographic findings and the method of examination are deemed worthy of report and brief description.

The case (Louisville City Hospital No. B63633) is that of a white boy aged 17 years, who was admitted to the hospital on January 21, 1935. The chief complaint upon admission was marked distention of the abdomen. The swelling had been first noticed 3 months earlier and had increased progressively until the patient felt a great deal of abdominal discomfort. During the 3 months before admission other symptoms appeared in about the following order: slight morning cough, shortness of breath, swelling of the face in the morning, weakness, drowsiness, sharp precordial pain on only two occasions, occasional nausea, occasional night sweats, tenderness over the abdomen (especially over liver and spleen), and slight weight loss. The family history was negative.

The physical examination at the time of admission revealed the presence of a large quantity of fluid in the peritoneal cavity, rather marked enlargement of the liver, barely palpable spleen. The pulse ranged from 80 to 100, respiratory rate 20 to 28, blood pressure 100/70, temperature 97 to 99 degrees F. The cervical nodes were palpable, tonsils large. The lungs were apparently normal. The heart was not enlarged (by percussion), there were no murmurs, no thrill, or friction rub. The heart rhythm was regular. Wenckebach's, Broadbent's, and Friedreich's signs were not observed. The heart shifted normally upon changing the position of the patient. The apex beat was neither seen nor felt. Examination of blood and urine gave no significant data. Electrocardiographic examination showed normal shift of electrical axis upon changing the position of the patient from one side to another.

It is apparent from the symptoms and examination that there were no very definite diagnostic data. Portal cirrhosis and tuberculous peritonitis were most seriously considered. A surgical consultant favored Pick's disease.

The usual roentgenologic procedures yielded results that were consistent with adhesive pericarditis, but were not definitely diagnostic. A film taken at 6 feet anode film distance is shown in Figure 1. The heart chest ratio was 12.4 to 29.3 centimeters. The contour suggests early rheumatic heart disease. When the chest was screened the heart shifted normally. There was no evidence of adhesions between the pericardium and diaphragm. The anterior mediastinum illuminated normally. There was some doubt in regard to pulsatory excursion of the several chambers of the heart as there often is in the very cases in which definite information in this respect is most desired.

It may be said parenthetically, that the medical department was at least hesitant to recommend surg-



Fig. 1. Teleradiogram (6 feet) of patient before operation. Heart chest ratio 4 to 49.5 centimeters. No diagnostic changes.

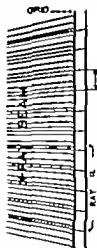


Fig. 2. Diagram designed to illustrate the purpose of the kymograph grid. The lead bands are 4 millimeters wide the slit between the bands, 4 millimeter. The grid runs points 4 millimeters apart on the lateral borders of the heart and great vessels and the downward movement of the film causes these pulsating points to be drawn into curves of characteristic form. If there were no movement of the heart, its borders would be represented by a succession of straight lines as shown in Figure



Fig. 3. Roentgenkymogram of normal heart. Note that the passive or filling phase is about two-thirds the length of the active or systolic phase. The maximum ventricular thrust is about 3 millimeters.

ical treatment for this patient, mainly I think, because of the lack of electrocardiographic evidence, whereas the surgical service was eager for diagnostic data that would clearly justify exploration of the pericardium.

At this time the author, as spending his evenings constructing a roentgenkymograph and while the device was nearing completion the surgeons are induced to withhold operation for a week on the bold promise that the new instrument could enable us to check the diagnosis. Roentgenkymograms of the patient were made on the day the instrument was installed, and the results of the examination justified our prediction.

Operation February 1934 confirmed our interpretation of chronic pericarditis. The adhesions were intrapericardial, not very dense but the pericardial sac was almost completely obliterated. The sections of pericardium removed were 1 to 3 millimeters thick, covered on the inner surface with shreds of connective tissue. The outer surfaces are normal.

Interpretation of the roentgenkymograms of the patient will be facilitated by examining first a kymogram of a normal heart (Fig. 2). The chest shadow is divided into transverse bands. The width of the bands represents the distance the film has moved downward during the exposure; in this case approximately 11 millimeters. The recording of the curves begins at the lower margins of the bands due to

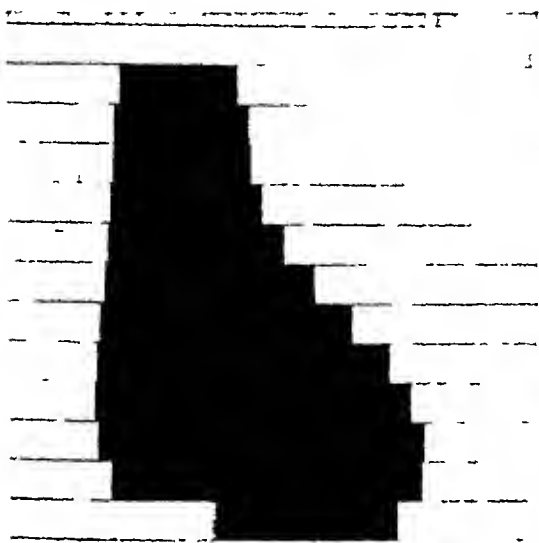


Fig 4 Roentgenkymogram in which a heart shaped sheet of lead has been substituted for a living subject. This shows clearly the straight line stepladder effect produced by a stationary object. The film moves downward during the exposure a distance slightly less than the width of the lead strips of the grid. The lower margins of the bands represent the beginning of exposure, the upper margins the end.

the fact that the motion of the film is downward. The "light" beam is fixed vertically by the grid (Fig 3) but can be "modulated" so far as transverse movement is concerned by any radio-opaque object that has movement parallel with the slits of the grid. The curves are therefore read from below upward. It must be borne in mind that an individual curve does not represent 11 millimeters of the cardiac border, but does represent the outward and inward thrust of the particular point on the cardiac border which lies in the line of a particular slit in the grid (Fig 3). This point is drawn out into curve form by the downward movement of the film. Obviously stationary objects or objects that move only upward and downward will be recorded as straight lines (Fig 4). The width of the band, and consequently the length of the curve, is determined by the width of the lead bands used in the construction of the grid. A narrow band grid naturally fixes a larger number of points on the cardiovascular margins, thus reducing the stepladder character of



Fig 5 Roentgenkymogram of patient before operation. The left ventricular border is represented by straight lines, indicating clearly the absence of the normal lateral thrust. Excursion of the left auricle is slightly increased. The aortic wave is greatly diminished, and no wave is seen on the right border. Compare with Figure 4.

successive bands (Fig 4). The band curves are produced by a shorter film movement. If the bands are too narrow the curves are very much compressed and finer details difficult of interpretation, although the cardiovascular contour is well preserved. A grid with wide bands will exaggerate the stepladder effect. The cardiovascular shadow will be outlined by a smaller number of fixed points, but the longer curves of slower progression will show finer details to better advantage.

With these facts in mind we may examine Figure 5 which is a roentgenkymogram of our patient. It is strikingly apparent that there is no lateral thrust or excursion of the left ventricle. Other sections of the cardiac shadow also show variations from the normals so far examined. The aorta shows only a slight ripple. The right border shows no movement. There is an augmented, abnormal curve in the region of the left auricle. Our interpretation of adhesive pericarditis was based upon the exclu-



Fig. 6. Roentgenkymogram of the patient 14 days after operation. There was considerable amount of fluid in the mediastinum and left pleural sac. Thrust of all chambers is increased above normal.

sion of other conditions which might produce a stationary left ventricular border. There were no signs of fluid in the pericardium. The duration of the disease and the severity of symptoms were against acute fibrinous pericarditis. The heart was not enlarged.

Figure 6 is a roentgenkymogram of the same patient taken 14 days after operative removal of a considerable portion of the thickened and adherent pericardium. Left ventricular excursion shown in this film is definitely greater than normal. There is a considerable amount of fluid in the mediastinum and left pleural sac which began to accumulate after operation. Following operation the heart shadow widened from 12.4 to 13.5 centimeters. The patient required no further withdrawal of fluid from the abdomen.

Figure 7 is a roentgenkymogram taken 33 days after operation and shows practically normal amplitude of excursion of the left ventricle. The aorta shows a curve of wide amplitude. There is also an increase in amplitude along the right border of the heart.



Fig. 7. Kymogram of the same patient 33 days after operation for removal of adherent pericardium. Almost complete resorption of pleural and peritoneal fluid. Ample excursion of all parts of cardiorespiratory shadow on screen considerably modified.

There are some features of the various curves that appear to vary somewhat from the normal but we feel that their consideration at this time would be premature.

Whether or not the roentgenkymogram will give as definite results in all cases of adhesive pericarditis cannot be answered at the present time. We believe that the method will be especially useful in this condition and that it will furnish positive diagnostic data in a large percentage of cases that would otherwise be recognized only at autopsy.

#### THE ROENTGENKYMOGRAPH

Those readers who are interested in obtaining a roentgenkymograph will find that the instrument is not at present available on the market. Although the method has been known for a good many years, it has received very little consideration as a practical aid in laboratory diagnosis. Dr. I. Seth Hirsch deserves a great deal of credit for bringing the method for x-ray to the attention of Ameri-

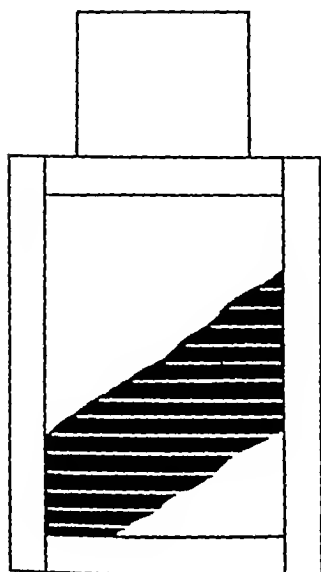


Fig 8

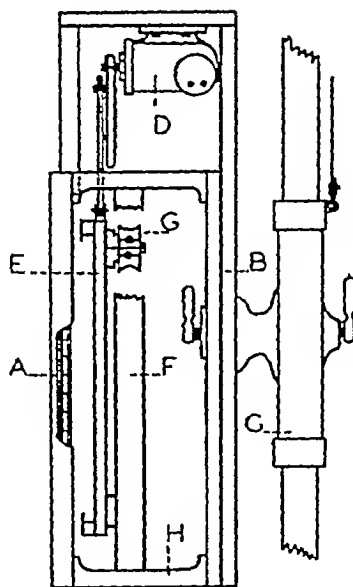


Fig 9

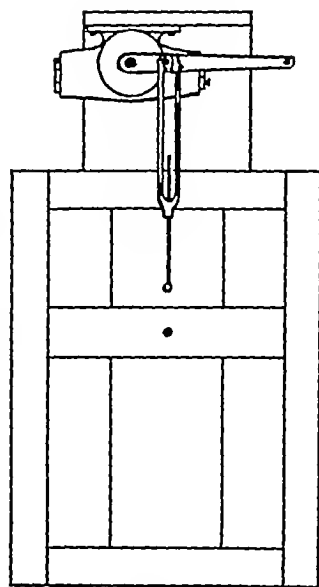


Fig 10

Fig 8 Front panel of kymograph consisting of wood frame, bakelite panel, lead strips  $\frac{1}{16}$  inch by 12 millimeters by 14 inches, paper spacers 0.4 millimeter thick, and  $\frac{1}{8}$  inch pressed wood back panel

Fig 9 Side view of complete assembly A, Front panel and grid, B, back frame, C, X ray tube stand, D, timing

device, E, cassette carriage, F, track (steel bar) for cassette carriage bearing, G, ball bearing on cassette carriage, H, aluminum casting

Fig 10 Back frame, showing position of 'timer' arms Note the change in the location of the ball joint on the main arm

can roentgenologists and for pioneer work in its further development

The kymograph described herewith was constructed by the author at a cost of about forty dollars and a reasonable amount of labor. There are no difficult mechanical operations involved in the construction as carried out by the writer. The item of greatest expense was a heavy old type tube stand which serves very well as an adjustable support.

The roentgenkymograph consists essentially of (1) the body or framework, (2) a movable cassette carriage, (3) a timing device, (4) the lead grid (5) an electric contact switch, and (6) a vertical support.

The body of the author's device was built of hardwood with strong mortised joints. There are two frames: a back frame (Fig 10) by means of which the instrument is attached to the swivel plate of the tube stand and a front frame (Fig 8) which supports the grid. The front frame is attached to the rear frame by means of four aluminum castings which serve as spacers and supports for two bilaterally

placed seven-eighths inch round steel bars. The steel bars form the track on which the cassette carriage is mounted by means of four ball bearings. The outer races of the bearings have half-round or V-faces in order to hold the cassette carriage in place (Figs 9, 11).

The cassette carriage is a wood frame, just the size of a 14 by 17 cassette. Strips of metal are attached to upper and lower borders to form a slideway for the cassette (Fig 9). The bearings are attached to the back of the frame at the corners (Fig 11). The fitting of the carriage to the track should be reasonably accurate to prevent wobble and at the same time permit its perfectly smooth movement.

The timing device used by the author is a No. 2 oil-cylinder door closer such as may be seen in any office building. The speed of action of this device can be regulated quite accurately by means of a needle valve which regulates the flow of oil from one cylinder to another. The device has a removable arm which is made up chiefly of a long turnbuckle. This is attached to the main arm or lever by a

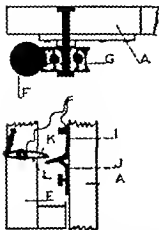


Fig. 1 above. Detail of cassette carriage bearing. G and track, F. 4. Cassette carriage frame.

Fig. 2 Detail of electric space switch. A. Front panel, K, cassette carriage and slider. I, brass hinge. J, sliding rest for lower lead of hinge. E, breaker arm. L, top pin.

ball joint. This joint was moved inward from the outer end of the arm about two-thirds of the length of the arm (Figs 9, 10). This gives a smaller arc and smoother action for the downward thrust. The outer end of the turnbuckle is attached to the top of the cassette carriage. The part of the main arm that projects beyond the new location of the ball joint serves as a hand lever for resetting the film carriage after an exposure has been made. The body of the "timer" is bolted to an elevated cross piece as shown in Figure 9.

The grid (Figs 3, 8) is the most important part of the roentgenkymograph and considerable care is required in its construction. The lead strips must be of uniform width and the spacing constant throughout the grid. With limited shop equipment, the author chose the simplest method of construction. A piece of  $\frac{1}{4}$  inch by  $\frac{1}{4}$  inch by  $\frac{1}{4}$  inch hand pressed board was used as a base. Lead bands  $\frac{1}{16}$  inch thick, 12 millimeters wide and 14 inches long were cut on a fine tooth band saw having first clamped a jointed guide on the saw table. This method produced less upsetting of the edges of the lead bands than other methods tried experimentally. Narrow strips of paper 0.4 millimeter thick were obtained from a print shop. These were used as spacers be-

tween the lead bands. Lead bands and paper strips were laid alternately in glue on the base board, until the grid was complete. The lead bands were easily straightened and trued up by means of a heavy straight edge. The spacing should be frequently checked with rule and square. When the glue was dry the paper showing above the lead was removed with a sharp scraper. The grid was completed by covering with a piece of  $\frac{1}{16}$  inch bakelite. The grid was then set in the front frame of the kymograph as shown in Figures 8 and 9. The grid is removable and interchangeable by withdrawing four screws. This feature is desirable since we do not as yet know what width band will prove most generally useful.

The electric contact is in reality a space switch. It is plugged into the hand-timer cable and its purpose is to turn on the X-rays after the cassette carriage has begun its downward motion and hold the current on for a predetermined space of travel of the cassette a distance slightly less than the width of the lead bands. The author's space switch is a very crude device consisting of a small brass hinge mounted on the frame and a pivoted brass arm attached to the cassette carriage (Fig. 12). The former is adjustable so that the "distance-exposure" can be varied to suit the width of the lead bands in the grid.

A heavy tripod tube stand completes the assembly. The kymograph is attached to the large face plate of the tube stand by a single bolt with a large hand screw. This permits turning the kymograph to the horizontal position as well as ready adjustment to the height of the patient (Fig. 9).

This description is offered in the hope that a considerable number of hospitals and clinics will have the instruments constructed and put into use. Only in this way can the practical value of roentgenkymography as a diagnostic method be established. That the method has practical diagnostic value seems assured. Anyone who is interested in the subject should read the excellent articles by Dr. Hirsch, mentioned. It is beyond the scope of this paper to review the literature on roentgenkymography. A complete bibliography will be found in Part II of Dr. Hirsch's paper.

EVIDENCE FOR THE PLACENTAL ORIGIN OF THE EXCESSIVE PROLAN OF LATE PREGNANCY TOXEMIA AND ECLAMPSIA<sup>1</sup>

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IN a series of 68 women in the second half of pregnancy, quantitative analyses of the serum and urine for prolan and estrin have shown that late pregnancy toxemia and eclampsia are characterized almost without exception by a marked excess of prolan as compared with normals. A low level of estrin in a large proportion of these patients has also been found, but the quantitative abnormality of this hormone is less striking and less consistent than that of prolan.

Both the placenta and the anterior lobe of the hypophysis are known to contain gonadotropic factors. The experiments to be reported were carried out for the purpose of determining which of these two sources is responsible for the excess found in late pregnancy toxemia and eclampsia.

## I TESTS ON HYPOPHYSECTOMIZED RATS

One of the biological means of distinguishing placental from hypophyseal prolan is based upon the differential effect upon the ovaries of hypophysectomized rats. Smith

(11) reports that replacement therapy by rat pituitary transplants into hypophysectomized female rats induces follicular growth and the formation of cysts which later luteinize. In contrast to this, the injection of pregnancy urine extracts (6), presumably placental prolan, into mature female rats 16 to 81 days after hypophysectomy causes an enlargement of the ovaries, a characteristic interstitial cell hypertrophy, and often the formation of corpora lutea, but no follicular activity.

In our experiments, mature virgin female rats were hypophysectomized<sup>2</sup> and not employed until at least 3 weeks after operation, when they were found to have lost weight and to be in constant diestrus. An estrin free saline extract of the alcohol-ether insoluble fraction of the materials used was prepared immediately before injections were started. *In every case the amount of material equivalent*

<sup>2</sup>We are much indebted to Dr. K. W. Thompson, Cushing Fellow in Surgery at the Peter Bent Brigham Hospital, who hypophysectomized the rats used.



Fig. 1 Atrophied ovary of hypophysectomized rat. Excised before starting injections of a placental extract. This and the following photomicrographs are all of the same magnification.

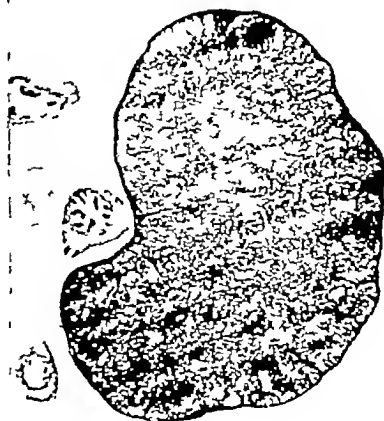


Fig. 2 Opposite ovary of the same rat as in Figure 1, 6 days later, after receiving 4 rat units of a gonadotropic placental extract. Note increase in size, interstitial hypertrophy and lack of follicular development.

<sup>1</sup>The Mrs. William Lowell Putnam Investigation of the "toxemias of pregnancy."





Fig 3 Atrophied ovary of hypophysectomized rat. Excised before starting injections of pituitary extract.

to 4 rat units of prolactin as determined on ten mature females was tested. The hypophysectomized rats were explored and only those with atrophied ovaries containing no corpora lutea were selected. One ovary was excised and sectioned for microscopic examination. The extract was given in 8 injections 2 a day for 4 days, and the rats explored on the sixth



Fig 4 Opposite ovary of the same rat as in Figure 3 6 days later after receiving 4 rat units of gonadotropic extract of sheep pituitaries. Note follicular development and corpora lutea.

day at which time the remaining ovary was excised and sectioned. Figures 3 and 4 show the result of the injection of 4 rat units of a gonadotropic extract of a full-term human



Fig 5 Atrophied ovary of hypophysectomized rat. Excised before starting injections of an extract of late pregnancy sera.



Fig 6 Opposite ovary of the same rat as in Figure 5, 6 days later after receiving 4 rat units of gonadotropic extract of late pregnancy sera. Note irregularity to Figure 4 and lack of follicular development. The same picture resulted from injections of extracts of both normal and traumatic late pregnancy sera.

placenta The picture is similar to that described by Leonard and Smith (6) when they employed a pregnancy urine extract, i.e., interstitial hypertrophy is the most marked reaction The uterus after injections remained small The rat from whom the sections shown in Figures 3 and 4 were obtained had received 4 rat units of a gonadotropic extract of sheep's hypophyses The uterus, after injections, was very cystic, and the difference in the ovarian reaction is apparent, i.e., Figure 4 shows an enlargement of follicles as well as corpora lutea The sera of 10 women in late pregnancy were extracted and tested Three of them were normally pregnant, 3 had eclampsia, 3 had pre-eclamptic toxemia, and 1 nephritis Figures 5 and 6 give a typical picture of the ovarian reaction to all of these serum extracts, an ovary characterized by hypertrophy of the interstitial cells Occasionally small corpora lutea appeared also In no instance were a cystic uterus or enlarged ovarian follicles found<sup>1</sup>

These results indicate that the gonadotropic hormone of all of the sera tested was placental rather than hypophyseal, and that the large amount of prolan found in the blood of these toxemic and eclamptic patients did not differ in its source from the prolan of the normally pregnant women and was presumably not due to excessive pituitary activity

## II QUANTITATIVE ANALYSES OF NORMAL TOXEMIC AND ECLAMPTIC PLACENTAS FOR PROLAN AND ESTRIN

If the high concentration of prolan in the blood and urine of toxemic and eclamptic women has its origin in the placenta, this fact should be demonstrable by comparative quantitative placental analyses With this idea in view we have extracted and analyzed 10 normal, 8 toxemic, and 5 eclamptic placentas

The methods used for extracting placentas undoubtedly do not give complete recovery of either prolan or estrin, but inasmuch as the same procedure was followed throughout, the results should be comparable For the purpose of getting check determinations as well as comparing the maternal and fetal portions,

the fresh placentas were sliced and the fetal third or half separated from the maternal third or half The specimens to be extracted were scraped as free as possible from blood vessels and connective tissue, spread on glass plates, and dried in a vacuum desiccator over calcium chloride for several days, when it was possible to grind them in a mortar to a very fine powder Two to 5 grams of each portion was accurately weighed into each of two 250 cubic centimeter centrifuge bottles, one to be used for the extraction of estrin and the other for prolan Twenty to 30 cubic centimeters of distilled water were then added and the materials left to extract in the refrigerator for 2 days with occasional stirring The bottles were then filled with 95 per cent ethyl alcohol

For the precipitation of prolan one bottle was then put back into the refrigerator overnight, centrifuged, the alcohol discarded, the precipitate washed with ether allowed to dry in the centrifuge bottle, and broken up to a fine powder with a stirring rod An amount of saline equivalent to 9 cubic centimeters per gram of dried placenta was added and the centrifuge bottle returned to the refrigerator for another 24 hours with frequent stirring of the contents The material was then centrifuged and the supernatant fluid used for testing on immature female rats in the same manner as that described for urine and serum extracts (10) The smallest amount of saline extract that produced grossly visible discrete corpora lutea was considered 1 rat unit

For the extraction of estrin the other centrifuge bottle was placed on the steam bath for 18 hours with frequent stirring, the alcohol centrifuged off and saved, and 100 cubic centimeters of fresh alcohol added for another 4 hours' extraction on the steam bath After centrifugation the insoluble residue was then washed with ether, centrifuged, and discarded The alcohol and ether supernatants were combined in a beaker and an amount of olive oil equivalent to 4.5 cubic centimeters per gram of dried placenta was added All of the alcohol and ether was evaporated off on the steam bath and the olive oil extract used for testing on spayed female rats in the same manner as that described for urine and serum extracts (10) The smallest amount of olive oil extract

<sup>1</sup>These photomicrographs were made by Dr. W. W. Boyd, to whom we wish to express our gratitude

TABLE I—QUANTITATIVE DETERMINATIONS OF PROLAN AND ESTRIN IN THE PLACENTAS FROM 10 NORMAL PREGNANCIES

Case	History	Date when due	Date of delivery	Clinical conditions	Placental prolan per mg. per gm.		Placental estrin mU. units per gm.	
					Maternal portion	Fetal portion	Maternal portion	Fetal portion
B. I. 1		8- -23	9-27-23	Twin normal			6	6
B. I. 2		8- -23	9-27-23	Twin normal				20
Mrs. J. T.	Aged 42 2 1/2 years 1st normal pregnancy Abortion		normal 8-23	Twin normal B P 120/70 Albumen			6	6
Mrs. J. L.	Aged 36 1 year	11-12-23	-18-23	Twin normal B P 120/70 Albumen		5	6	2
Mrs. J. B.	Aged 37 1 1/2 years Last pregnancy normal	1- 4-23	2-12-23	Twin normal B 100/70 Albumen			3	6
Mrs. V. M.	Aged 27 1 year	11-16-23	1-17-23	Twin normal B P 100/70 Albumen			3	
Mrs. C. G.	Aged 30 1 year	10-17-23	11-12-23	Twin normal B P 100/70 Albumen			6	6
B. L. 1		6- -24	6-27-24	Twin normal			6	6
Mrs. T. W.	Aged 29 1 year	1-18-24	2-17-24	Twin normal B P 90/70 Albumen			20	20
Mrs. J. A.	Aged 24 1 year	1-18-24	2-17-24	Twin normal B P 120/70 Albumen			20	
Average figures					6 1/2	4 1/2	6 30	20

that produced full estrous smears in half the rats injected was considered 1 rat unit. The results for both prolan and estrin are expressed in rat units per gram of dried placenta.

The results of the analysis of 10 full term normal placentas are given in Table I. The maternal and fetal values check within the limits of experimental error for both prolan and estrin. The prolan of these 10 placentas lies between 1 and 4.5 rat units per gram of dried tissue and the estrin between 3 and 12 rat units.

Table II presents the results on the placentas from 8 cases of late pregnancy toxemia. The average figures for placental prolan are considerably higher than those of the 10 normal placentas and in every instance the prolan of the maternal portion exceeds the highest normal amount. It is interesting to note

W. have found that about 3 grams of wet tissue yields 1 gram of dried powder. In terms of wet weight therefore the portion of these 10 normal placentas lies between one and one rat units per kilogram, and the estrin between two and 20 mU. Also reports the finding of between one and two rat units of estrin per kilogram in normal human placentas.

that in half of these cases the maternal portion of the placenta contains appreciably more prolan than does the fetal. This may be due to a less complete removal of blood vessels and connective tissue from the fetal part when preparing the materials to be dried and powdered. In Cases 11 and 14 such an explanation would be indicated since the maternal portions also contain more estrin than do the fetal. (The estrin and prolan extracts were always made up from weighed amounts of the same sample of dry powder.) In Cases 15 and 17 however the maternal and fetal portions give the same yields of estrin, so that the larger amount of prolan in the maternal as compared with the fetal portions in these 3 cases would seem to be a real excess such as was not found in any of the normal placentas.

Half of these 8 toxemic placentas contain less estrin than was found in any of the normal and the average figures are appreciably lower. These results are comparable with

TABLE II—QUANTITATIVE DETERMINATIONS OF PROLAN AND ESTRIN IN THE PLACENTAS FROM 8 CASES OF LATE PREGNANCY TOXEMIA

Case	History	Date when due	Date of delivery	Clinical diagnosis	Placental prolan rat units per gm		Placental estrin rat units per gm	
					Maternal portion	Fetal portion	Maternal portion	Fetal portion
11 Mrs. E.D.	Aged 32 VII para Toxemia with last pregnancy	9-2-33	9-11-33	Term Toxemia without convulsions B.P. 128/102 Albumin slight trace Edema	90	30	30	15
12 Mrs. M.*	Aged 33 II para Toxemia with last pregnancy	8--33	Induced 7-33	Term Toxemia without convulsions B.P. 140/95 Albumin slight trace Edema	60	60	60	60
13 Mrs. McG.	Aged 32 II para Toxemia with last pregnancy	10-10-33	10-16-33	Term Toxemia without convulsions B.P. 140/100 Albumin slight trace Edema	60	60	15	15
14 Mrs. McI.	Aged 30 VII para Previous pregnancies normal	1-10-34	12-29-33	Term Toxemia without convulsions B.P. 156/90 Albumin slight trace	120	60	60	30
15 Mrs. D.	Aged 36 I para Previous pregnancies normal	12-23-33	1-1-34	Term Toxemia without convulsions B.P. 140/75 Albumin o Edema	120	20	60	60
16 Mrs. F.	Aged 3 I para	5-13-34	--7-34 by cesarean	8 months Pre-eclamptic toxemia B.P. 170/120 Albumin light trace Headaches	300	300	30	15
17 Mrs. M.R.	Aged 40 VIII para 7 normal pregnancies 3 miscarriages Elevated blood pressure with last pregnancies	--9-34	7-10-34 by cesarean	8 months Pre-eclamptic toxemia B.P. 190/110 Albumin light trace Blurred vision	300	120	60	60
18 Mrs. M.F.	Aged 41 VI para Previous pregnancies normal	8-1-34	7-27-34	8½ months Toxemia without convulsions B.P. 230/100 Albumin heavy trace Edema	90	120	>15	>15
Average figures					142	96	41	33

\*Case 7 of the preceding paper

†Case 13 of the preceding paper

‡Case 15 of the preceding paper

Serum prolan 500 r.u./100 c.cm. at 8 months  
 Serum estrin 50 r.u./100 c.cm. at 8 months.  
 Serum prolan 500 r.u./100 c.cm. at term  
 Serum estrin less than 33 r.u./100 c.cm. at term  
 Serum prolan 500 r.u./100 c.cm. at delivery  
 Serum estrin less than 20 r.u./100 c.cm. at delivery

those for serum estrin in toxemic cases, as would be expected, since the placenta has been accepted as the principal source of estrin in late human pregnancy (12, 13)

In the 8 placentas of Table II, the degree of imbalance between prolan and estrin runs roughly parallel to the severity of the symptoms. Cases 16 and 17 are the only two with a clinical diagnosis of pre-eclamptic toxemia, and their placental prolan is more than twice

that of any of the other 6 with a less certain clinical diagnosis. Case 18 had more severe symptoms than did 11, 12, 13, 14, and 15 and, although her placental prolan was no higher than that of Cases 14 and 15, her estrin level both in the blood and placenta was exceptionally low, indicating a marked imbalance. These results would certainly favor the conclusion that the high level of prolan found in cases of late pregnancy toxemia, as well as the

TABLE III—QUANTITATIVE DETERMINATIONS OF PROLAN AND ESTRIN IN THE PLACENTAS FROM 5 ECLAMPTICS

Case	History	Date when due	Date of delivery	Clinical diagnosis	Placental prolan net units per gm		Placental estrin net units per gm	
					Maternal portion	Fetal portion	Maternal portion	Fetal portion
19 Mrs. A.	Acid 21 VIII para All previous pregnancies normal	3-7-34	3-7-34	Turn Eclampsia—two tox volumes B P 160/120 Albumin, heavy trace	3	1	3	
20 Mrs. M. S.	Acid 26 I para	4-1-34	3-27-34	Turn Eclampsia—two tox volumes B P 160/120 Albumin, heavy trace		6	3	
21 Mrs. B.	Acid 26 VI para Lentation with last pregnancy. This pregnancy normal until 3 weeks ago Preeclampsia and eclampsia later	6-7-34	5-27-34	Turn Eclampsia—five tox volumes B P 160/120 Albumin, heavy trace	180	43		3
22 E. M. A.	Acid 27 I para	?	8-26-34	3 months Eclampsia—several convulsions and death B P 160/120 Albumin, heavy trace	30	14		
23 M. S.	Acid 21 VII para All previous pregnancies normal	10-34	6-7-34	3 months Eclampsia—five tox volumes B P 160/120 Albumin, heavy trace	30			3
Average figures					66	16		

\*Case 18 of the preceding paper

Serum prolan 200  
 Serum estrin 15  
 Serum prolan 1000  
 Serum estrin 15  
 Serum prolan 1000  
 Serum estrin 15

†Case 19 of the preceding paper

1/100 Cn at birth  
 1/100 Cn at birth  
 1/100 Cn at birth  
 1/100 Cn at birth

‡Case 24 of the preceding paper

1/100 Cn at birth  
 1/100 Cn at birth  
 1/100 Cn at birth  
 1/100 Cn at birth

tendency toward low levels of estrin originate in a placental abnormality

The placentas of 5 patients with eclampsia have been analyzed and the results are given in Table III. In 3 of these the prolan is markedly higher than normal and the exceptionally high prolan of one of them accounts for the height of the average figures. In these 3 placentas also the excess of prolan is more marked in the maternal than in the fetal portions. In all 5 of them a somewhat low level of estrin is apparent.

The placentas of Cases 19 and 20 contain amounts of prolan that are only on the high side of normal. Case 19 also had a less marked excess of serum prolan than would be expected in an eclamptic, and it was suggested in the discussion of this case in the preceding paper that by the time the symptoms of eclampsia appear placental changes may take place which result in a decreased production of this hormone as well as of estrin. The weight of

evidence in our quantitative studies of estrin and prolan has favored the conclusion that the low estrin levels follow rather than precede the excessive production of prolan. It is logical to assume that if the disease causes placental damage with decreased production of estrin, the prolan production would also be decreased so that the values for both of these hormones, by the time symptoms appear would be considerably lower than at an earlier date. Case 18 is a case in point. The exceptionally low estrin both in the blood and placentas of this patient, as well as the fact that her prolan levels were not as high as would be expected considering the severity of her symptoms, have been commented upon. Perhaps the correct interpretation of all the cases in which low levels of estrin were more marked than excess of prolan would be that these findings indicate placental damage.

On 6 of the women whose placental analyses are reported in Tables II and III, serum deter-

TABLE IV—QUANTITATIVE ANALYSES OF CONTROL TISSUES FOR PROLAN AND ESTRIN

	E. M. K. Eclampsic (Ca & 22 Table III)		Mrs S. Eclampsic		Mrs B. 5 months miscarriage	
	Prolan	Estrin	Prolan	Estrin	Prolan	Estrin
Serum—r u. per 100 ccm	1430					
Placenta r u. per gm						
Maternal portion	700	30			90	100
Fetal portion	190	30			30	100
Liver—r u. per gm	0	15	0	0		
Spleen—r u. per gm	0	0	0	0		
Kidney—r u. per gm	30	15				
Fetal liver—r u. per gm					0	20
Fetal brain—r u. per gm					0	0

minations were also run. The serum and placental figures for prolan do not always run parallel. This is especially apparent in Case 18 in which the excess of prolan in the placenta is much more marked than in the serum, and in Case 20 in which the opposite situation is found. It has been pointed out before (10) that the ratio of prolan in the urine to that in the serum is not as constant in cases of toxemia and eclampsia as it is in normal pregnancies. All of these inconsistencies may be accountable to interfering substances in the materials analyzed, resulting in unavoidable sources of error in the present methods of extraction. Another possibility is that they may be due to differences in the ability to excrete prolan. Excessive production of prolan by the placenta would not result in a correspondingly high serum prolan if the kidneys were able to excrete it. On the other hand, if the kidneys had been damaged a retention of prolan in the blood would result, even though the placenta, by the time of delivery, was not producing a marked excess.

In order to be certain that the high prolan and low estrin in these placentas originate in that organ, control tissues from 2 women who died of eclampsia have been dried, extracted, and analyzed in the same manner as that described above (Table IV). Philipp has shown that the hypophyses of pregnant women are gonadotropically inactive, and the results in Table IV demonstrate that the liver, spleen, and kidneys of eclampsic patients do not contain amounts of these hormones comparable with those found in the blood and placenta.

Similar comparative analyses of the placenta and the fetal tissues of a 5 months' miscarriage (Table IV) have shown that the fetus is not the source of either prolan or estrin. These control experiments strengthen the hypothesis that the origin of prolan and estrin in both normal and toxemic pregnancies is in the placenta.

#### EVALUATION

Anselmino and Hoffmann have reported the finding of a "pituitrin-like" substance in the blood of toxemic and eclampsic patients which they believe to be responsible for these conditions. Cushing has made careful pathological studies of the pituitaries of a number of patients who died of eclampsia and has found in them the basophilic invasion from the pars intermedia into the posterior lobe which he considers characteristic of hypertensive disorders. These two reports certainly point toward pituitary dysfunction in cases of late pregnancy toxemia and eclampsia, and Cushing presents the general hypothesis that "the extent of basophilic invasion from the pars intermedia is a measure of posterior lobe activity and that excessive infiltration [of the posterior lobe] by these elements represents the histopathological basis of eclampsia." Since the experiments that we have reported seem to rule out the pituitary and point to the placenta as the source of the excessive prolan in these cases, the question arises as to how our findings fit into this latest theory as to the etiology of these conditions.

It is, of course, possible that pituitary changes might cause an overproduction of

TABLE III—QUANTITATIVE DETERMINATIONS OF PROLAN AND ESTRIN IN THE PLACENTAS FROM 5 ECLAMPTICS

Case	History	Date when died	Date of delivery	Clinical diagnosis	Placental prolan net weight per gm		Placental estrin net weight per gm	
					Maternal portion	Fetal portion	Maternal portion	Fetal portion
19 Mrs. A. K.	April 15 1 III para (All previous pregnancies normal)	3-14-34	3-23-34	Ten Eclampsia—two convulsions R F. 20/100 Albumen, heavy trace			1	1
20 Mrs. B. K.	April 16 1 para	4-2-34	3-20-34	Ten Eclampsia—two convulsions R F. 20/100 Albumen, heavy trace				
21 Mrs. C.	April 16 VI para Previous two last pregnancies. This pregnancy several weeks ago hemorrhages and eclamptic attacks	4-2-34	3-23-34	Ten Eclampsia—two convulsions R F. 20/100 Albumen, heavy trace	130	45		
22 Mrs. D.	April 17 2 para	7	4-27-34	1 month Eclampsia—several convulsions and death R F. 100/100 Albumen, light trace	30	15		
23 Mrs. E.	April 18 VII para (All previous pregnancies normal)	20-34	4-23-34	4 months Eclampsia—two convulsions R F. 20/100 Albumen, heavy trace	30			
Average figures					60	14		

\*Case 19 of the preceding paper  
 \*Case 20 of the preceding paper  
 \*Case 21 of the preceding paper

Serum prolan 400  
 Serum estrin 11  
 Serum prolan 3000  
 Serum estrin 11  
 Serum prolan 14,000  
 Serum estrin 30

400 mg. at birth  
 1000 mg. at birth  
 1000 mg. at birth  
 1000 mg. at birth  
 1000 mg. at delivery  
 1000 mg. at delivery

tendency toward low levels of estrin, originate in a placental abnormality.

The placentas of 5 patients with eclampsia have been analyzed and the results are given in Table III. In 3 of these the prolan is markedly higher than normal and the exceptionally high prolan of one of them accounts for the height of the average figures. In these 3 placentas also the excess of prolan is more marked in the maternal than in the fetal portions. In all 5 of them a somewhat low level of estrin is apparent.

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evidence in our quantitative studies of estrin and prolan has favored the conclusion that the low estrin levels follow rather than precede the excessive production of prolan. It is logical to assume that if the disease causes placental damage with decreased production of estrin the prolan production would also be decreased so that the values for both of these hormones, by the time symptoms appear would be considerably lower than at an earlier date. Case 18 is a case in point. The exceptionally low estrin both in the blood and placenta of this patient as well as the fact that her prolan levels were not as high as would be expected considering the severity of her symptoms, have been commented upon. Perhaps the correct interpretation of all the cases in which low levels of estrin were more marked than excessive prolan would be that these findings indicate placental damage.

On 6 of the women whose placental analyses are reported in Tables II and III, serum deter-

other placental abnormality which as yet remains unknown<sup>1</sup>

#### SUMMARY AND CONCLUSIONS

The sera of women with late pregnancy toxemia and eclampsia have been found to have the same effect upon the ovaries of hypophysectomized rats as the sera of normally pregnant women. An extract of human placenta also had this effect while hypophysectomy caused a follicular and luteal activity not caused by any of the other materials tested.

Quantitative analyses have shown that the placentas of toxemic and eclamptic patients contain excessive amounts of prolactin and tend toward low levels of estrin as compared with the placentas of normal pregnancies.

Control tissues from 2 women who died of eclampsia and 1 who miscarried at 5 months have shown that the liver, spleen, kidney, and fetus contain practically no prolactin or estrin.

It is concluded that the excessive amounts of prolactin previously reported (10) in the

blood and urine of toxemic and eclamptic women as well as the tendency toward low levels of estrin have their origin in the placenta.

It is suggested that a continued overproduction of prolactin by the placenta is probably a related factor and possibly causal in the etiology of late pregnancy toxemia and eclampsia.

NOTE.—Since this paper was submitted for publication 8 more placentas have been analyzed and the findings are consistent with the data herein tabulated.

#### BIBLIOGRAPHY

1. ALLI, F. D. Chapter X in Sex and Internal Secretions, 1932.
2. ANSTUHL, O. K. J. HOFFMANN, F. and KENNEDY, W. P. Edinburgh M. J. 10, 31, 37.
3. CUSHING, HARVEY. Am. J. Path. 19, 10, 173.
4. KATZ, P. A. and DUBOIS, L. A. J. Biol. Chem. 1934, 10, 1-5.
5. KAUFMAN, C. and MEHLBOCK, O. Klin. Wochenschr. 10, 12, 1450.
6. LEONARD, S. L. and SMITH, PHILIP I. Proc. Soc. Exper. Biol. & Med. 1935, 30, 1-45.
7. NOVAK, F. and KOFF, A. K. Am. J. Obs. & Gynec. 1930, 20, 451.
8. PHILIPP, I. Zentralbl. f. Gynaek. 1930, 54, 30.
9. SILVERMASTER, A. F. Proc. Soc. Exper. Biol. & Med. 1934, 31, 593.
10. SMITH, G. V. and SMITH, O. W. Am. J. Physiol. 1934, 107, 1-5.
11. SMITH, P. F. From Allen Edgar Sex and Internal Secretions. Baltimore: The Williams & Wilkins Co., 1932.
12. SZARAS, S. Zentralbl. f. Gynaek., 1930, 54, 2-11.
13. WALDSTEIN, Zentralbl. f. Gynaek. 1920, 53, 1303.
14. WOLFE, J. M., PHILIP, D. and CLEVELAND, P. Proc. Soc. Exper. Biol. & Med. 1933, 30, 1002.
15. ZONDEL, B. Klin. Wochenschr. 1931, 10, 121.

It is interesting to note that in the case of late pregnancy toxemia and eclampsia we have been able to find a similarity between the condition and the menopause. A characteristic low level of estrin (the amount of menstruation) has been reported by many writers and is noted in this laboratory. The level of prolactin is also low in the urine of menstruating women. This has been frequently reported (4, 5, 6) and also by some writers who have not been able to find it. We have found it consistently in women with normal cycles who we have studied throughout three years of menstrual periods. Moreover, an increase in weight at the time of the period has recently been reported which with the estrin of late pregnancy might be due to the same endocrine state in. And in late pregnancy increased capillary permeability with hemorrhage is characteristic of both toxemia and menstruation although in the latter the blood is not coagulated. We have stated in our paper on the parathyroid gland that we do feel that the idea of what might be called a "late pregnancy" but we do feel that the idea of what might be called a "late pregnancy" associated with low estrin and high prolactin in the blood may be worthy of consideration.



# CLINICAL SURGERY

FROM THE UROLOGIC SERVICE, HIGHLAND HOSPITAL

## LATERAL APPROACH FOR OPERATING UPON DIVERTICULA OF THE BLADDER

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THE standard approach for operating upon diverticula of the bladder is through a midline suprapubic incision. There are times, however, when it is more advantageous to use a pararectus approach. This would apply especially in cases in which the diverticulum is situated on the side of the bladder or when the neck of the diverticulum is at the inferolateral angle. Judd (17) reminds us that "The difficulties of the operation lie in separating the sac from the surrounding tissues, especially if the sac is thick walled, and if there is a great deal of old infection and scar tissue. The vas deferens and the ureter both of which will come into view in many of the dissections, should always be avoided."

By use of the lateral approach the operation can be done entirely extraperitoneally and extravesically requiring only one artificial opening into the bladder which is produced by severing the diverticulum from its junction with the bladder. This opening can be sewed together enough room being left to introduce a rubber drainage tube into the bladder. This does away with a second opening in the dome of the bladder which is made if the midline abdominal incision is used and a combined intravesical-extravesical operation is done.

The incision is a modified Gibson hockey-stick which he first described in 1903 as an approach for extraperitoneal arteriotomy. It is a pararectus incision down to within an inch above Poupart's ligament where it turns a sharp angle toward the midline of the abdomen. The exposure is much roomier than through the standard midline incision and is of great help in cases in which the diverticulum is firmly adherent to the surrounding structures due to an old peridiverticulitis. The advantage here is that the surgeon can see and separate the outside of the sac by blunt or sharp dissection from the rectum and peritoneum. The ureter can be identified and iso-

lated several inches above the diverticulum, and followed down to its ultimate entrance through the bladder base. This may necessitate dissecting free the ureter from dense adhesions to the diverticular wall. By this means a ureter may also be followed into, or through a diverticulum.

If the ureter is so densely adherent to the wall of the diverticulum that there is danger of tearing the ureter, sharp dissection can be used, and a narrow shelving edge of diverticular wall allowed to remain on the outside of the ureter. This is much easier than having to transplant the ureter which may be dilated or suffering from inflammatory ureteritis. It is not necessary to insert the drainage tube in the midline of the dome of the bladder. This tube may be inserted into the bladder through the diverticular neck, as shown in the diagram. Healing will take place properly and in the usual length of time, if the vesical neck has been freed from obstruction at a previous operation, usually by the transurethral route.

Since the use of the cystoscope and urogram has become routine vesical diverticulum is diagnosed much more frequently than in former years. Since the main symptoms are the same as those due to obstruction at the vesical neck, we have to differentiate diverticulum from prostatic disease due to hypertrophy, carcinoma, bar formation or contracture of the vesical neck. A complete study will reveal whether or not the obstruction at the vesical neck is complicated by the presence of a diverticulum. This is important, as it is imperative to relieve the vesical neck obstruction before excision of the diverticulum is planned. This point has recently been emphasized by Davis.

Hinman (3) has aptly described the *modus operandi* of how a diverticulum caused urinary obstruction. He says: "All of the larger diverticula were forced to direct their way posteriorly between the rectum and the prostatovesical

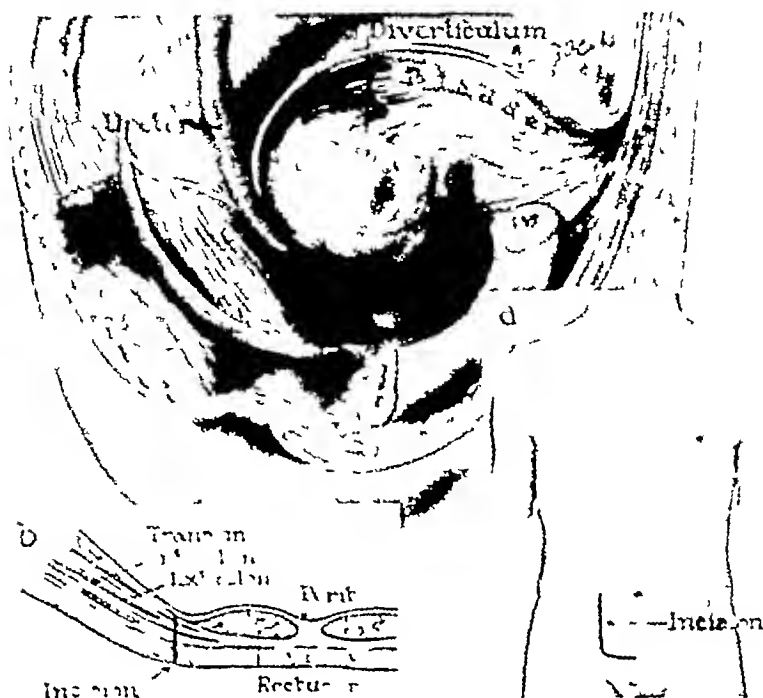


Fig. 1. Diagram showing relationship of the diverticulum to the bladder and the ureter adherent to base of diverticulum. a Incision. b section through abdominal wall at middle of incision.

region. This is probably the mechanical result of intra-abdominal pressure. At operation the sacs seemed to hang as by gravity from their necks so that upon distention they would force the posterior wall of the bladder upward, and when of large size would occasion marked obstruction to urination in very much the same manner as intravesical hypertrophy of the prostate itself.

In the extravascular technique as illustrated in this article all important structures are visualized, especially the relationship of the ureter to the diverticulum. A ureteral catheter is first introduced into the ureter through the cystoscope further to help in the identification of the ureter.

The disadvantages of the intravesical technique may be briefly summarized as follows:

a. Most of the diverticular sacs suffer from accompanying peridiverticulitis which causes them to be adherent to the surrounding structures.

b. The ureter is very frequently adherent to the outside of the diverticulum, or may even traverse it so that the ureteral orifice opens within the diverticulum, the corner of the trigone having been pulled up and into the diverticulum. When

this occurs, it becomes easy to cut across the ureter accidentally, which would require ureter transplant back into the bladder, after the diverticulum had been removed. On account of the severe infection in these cases, ureteral transplantation has been notorious for bad results frequently requiring later nephrectomy.

c. The diverticulum may be partly intraperitoneal, and upon inversion into the bladder by suction or traction forceps may contain a loop of bowel. If one is not especially careful here, he may cut into the peritoneum, or into the bowel, either of which would be a serious complication.

#### CASE REPORT

P. G., male, aged 59 years, was admitted to the hospital with the complaint of bloody urination of 3 weeks' duration. For about a year he had frequency, nocturia and dysuria with occasional difficulty in starting the urinary stream, but never any attacks of acute retention. The blood was intimately mixed with the urine and on several occasions contained small clots, but there was no voluminous hemorrhage at any time. The past history was irrelevant.

Physical examination was negative, except for the urinary system. The kidneys were neither palpable nor tender. The prostate, per rectum, was about normal in

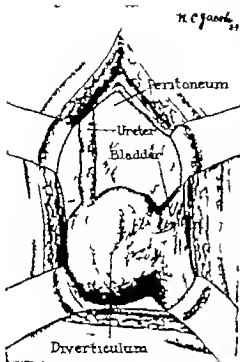


Fig. A wide exposure is easily obtained when the lateral incision is used.

size, shape, and consistency. The voided urine contained gross blood and pus. The blood non protein nitrogen was 30 milligrams per 100 cubic centimeters. 1 blood, and the phosphotungstic acid test collected at 30 minute intervals yielded 30, 5 and 10 for total of 67 per cent.

Cystoscopic examination showed an acute, diffuse cystitis, with well established leucoplakic change surrounding large diverticular opening on the right bladder base. There was definite fibrous contracture of the vesical neck. Contrast cystograms and retrograde pyelograms showed diverticulum almost the size of the bladder to the right of the midline, and bilateral hydronephrosis, and hydroureter. The urinary secretion through the ureteral catheters was clear and uninfected.

First operation consisted of bilateral vasectomy, and transurethral resection, two large plugs of tissue being removed from the base of the vesical neck. The patient refused operation for removal of the diverticulum, and was discharged. He returned 4 months later at which time diverticulectomy under spinal anesthesia was carried out.

**Operation.** The patient was cystoscoped and ureters No. 8 French ureteral catheter was passed into the right ureter and fastened to the penis with adhesive tape. A right paramedian incision was made from the level of the umbilicus down to an inch above Poupart's ligament, and then continued at sharp right angle to the midline of the abdomen. The incision was carried down to the peritoneal fat, but not into the peritoneum. The peritoneal sac was stripped away from the parametria, exactly as in the operation for extraperitoneal ureterotomy. The spermatic cord and its structures were identified and retracted

laterally. The diverticulum was easily found, densely adherent to the surrounding structures, and the ureter readily identified, with the ureteral catheter palpable through its wall. The lower reaches of the ureter was so firmly adherent to the diverticulum that it had to be separated by sharp dissection. The diverticulum was cut off where it joined the bladder leaving an opening twice as large as thumb. This was sewed together, except the upper angle through which DePesser catheter was inserted to act as cystostomy drain. The usual peritoneal deep closing was controlled by tamponing with long pack gauze pack. Closure was done in layers.

Postoperative reaction was very satisfactory. The gauze pack was slowly removed so that it was all out on the third day. The abdominal wound healed by primary intention, and the cystostomy tube was removed on the fourteenth day. One week later the cystostomy stoma had healed, and the patient voided large quantities of urine freely and easily per urethra. He was discharged at the end of the fourth week.

The pathologic report by Dr. N. W. Pope stated, A diverticulum of the urinary bladder 3 by 3 by 3 inches was submitted. The wall of the diverticulum under the microscope appeared to have the structure of the wall of the bladder, being composed of all the layers, mucosa, submucosa, muscular coat, and serosa. The epithelium was slightly thickened, otherwise as free of pathology. The mucosa showed no evidence of chronic inflammatory reaction. The muscular coat appeared thin in some areas. There was present marked edema of the serosa coat. The picture was that usually found in the congenital type of diverticulum.

#### DISCUSSION OF VARIOUS OPERATIVE PROCEDURES

**Extravesical.** The bladder is incised, and the opening or neck of the diverticulum is found. The diverticulum may be packed with gauze, or traction may be exerted by fingers inserted into the sac, and the dissection can be made by bimanual manipulation. Large diverticula are almost always adherent to the ureter. A ureteral catheter inserted into the ureter will assist in the identification, and aid in avoiding injury. Hyman does this through ureterotomy incision at the time of operation. It is sometimes easier to introduce a catheter through a cystoscope, which would obviate the necessity of cutting into the ureter. The diverticulum is dissected free from the surrounding tissue, and excised at the neck. It is usually advisable to place a drain in the perivesical space at the point where the sac was dissected free. The bladder is then temporarily drained by means of a catheter inserted through a suprapubic incision.

**Transvesical.** If there is evidence of marked perivesical inflammation, or if the bladder has been previously drained and there is much scar tissue, making extravesical dissection difficult and hazardous because of the possibility of opening the peritoneal cavity the transvesical method may be used. The wall of the diverticulum is

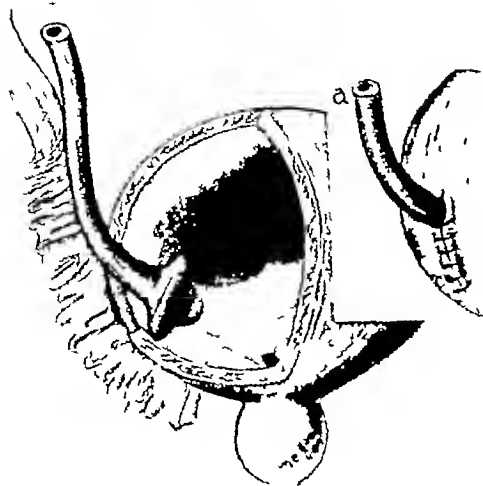


Fig. 3 Detail of drainage and extravascular gauze pack  
a. Closure of diverticular neck around drainage tube

made up of two main layers. These are the mucosa and an outer fibrous layer between which there are sometimes a few muscle fibers. The bladder is opened suprapubically and a good exposure of the diverticular opening is obtained. A circular incision is then made around the neck of the diverticulum through the bladder. The fibrous ring may also be incised in any direction in order to facilitate manipulation in dissection. The entire diverticulum is removed by a process of sharp, combined with blunt, dissection. A Penrose drain may be placed temporarily to the outer side of the bladder, and a No. 30 catheter is placed into the bladder for suprapubic drainage.

**Intravesical.** The method discussed by Young in 1906 has its virtue in that the mucous membrane can be separated from the wall of the sac rather easily in some cases. The procedure is usually applicable to the treatment of rather small diverticula. In cases in which infection is present around the sac, resort must be had to one of the two former methods—extravesical or transvesical. The bladder is opened suprapubically and the opening of the diverticulum is exposed. A pair of forceps is passed through the opening of the diverticulum and the fundus is firmly grasped. Traction with the forceps is made toward the interior of the bladder, and the sac is inverted into the bladder. The sac is then cut off at the neck, and the neck closed by sutures. A drainage tube for urine is placed into the bladder and the bladder closed around it.

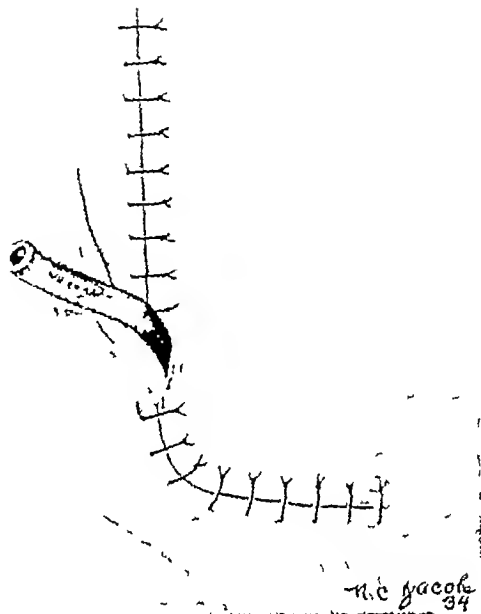


Fig. 4 Operation completed

In addition to the above three methods outlined by Walters (30) is the inversion of the diverticular sac into the bladder by the hollow glass tube and suction method originated by Hugh Young (32, 33).

**Geraghty's method.** A circular incision is made around the neck of the diverticulum and the mucous membrane lining of the diverticulum is separated bluntly from the outer fibrous layer of the diverticular wall. This leaves the fibrous layer of the diverticular sac still present, but Geraghty claims that the sac will obliterate itself in time. He then sutures the diverticular opening together within the bladder except for a small rubber tube which is passed through the diverticular opening down to the bottom of the sac for temporary drainage. He also drains the bladder suprapubically.

**O'Day's method.** He uses the intravesical approach, with elliptical excision of the diverticular neck. Closure of the excised neck with Murphy's watershed suture.

**Read's method.** The conservative treatment consists first, of removing the obstruction to the free passage of urine (prostate, median bar, stricture, etc.), second, in the dilatation of the mouth of the diverticulum, and an attempt to

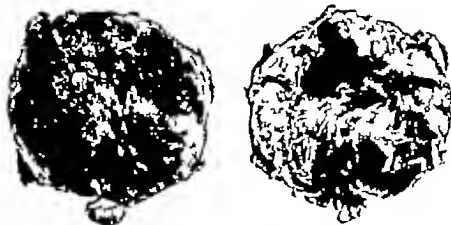


Fig. 5 Photograph of diverticulum, external and medial aspects.

prevent its recontraction. Through a suprapubic opening a free exposure of the diverticulum is secured. Its mouth is thoroughly dilated with the fingers. With the high frequency knife the fibrous ring is incised radially completely through its thickness. These incisions are made in three or four places. The value of this particular form of cautery is that it does not leave the thick scar of the actual cautery.

*Eisenstadt's method* In this method the diverticulum is exposed and separated as much as

possible from the surrounding structures. If the entire diverticulum can be isolated, it is cut away from the bladder by circumscision at its neck, and the neck closed by sutures. The bladder is then drained suprapubically. If the entire diverticulum cannot be isolated on account of firm adhesions, the bladder wall is incised from the suprapubic opening down to and including the diverticular neck. The diverticulum is then cut lengthwise and by means of a finger in the diverticulum to facilitate the separation of its



Fig. 6 Urogram showing catheter in the diverticulum, and left hydroureter.

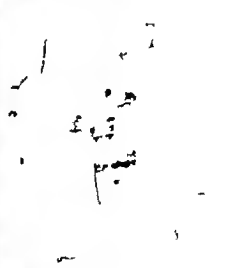


Fig. 7 Urogram showing catheter in the diverticulum, and right hydroureter.



Fig. 22



Fig. 23



Fig. 24

Fig. 22. Lateral roentgenograms of foot shown in Figure 21. There is equinus deformity of both the forefoot and ankle. The midline of the os calcis instead of pointing upward and forward points downward and forward. The astragalus points almost straight downward, almost parallel with the projected midline of the tibia.

Fig. 23. Anterior view of feet after correction of the forefoot adduction and the inversion. The feet are now ready to be brought up in dorsiflexion. The correction has been obtained by casts and wedgings.

Fig. 24. Lateral view of feet after they have been wedged in dorsiflexion for several weeks. Correction has been obtained very slowly. An Achilles tendon lengthening is to be done next.

when the feet were not stretched over a triangular block, and when no wrench was used. These children ended with rigid feet, and to be honest in evaluating the end results, I think their handicap was greater after the treatment than it was before. It was such cases as these which made me willing to take more time and expend more effort in getting better feet. This point is illustrated by the following case.

W. B. F. was carried to a skilled orthopedist when she was 3 weeks old. A series of casts were applied until she was 6 months old. At the age of 6 months she had an anesthetic and bilateral Achilles tendon lengthenings and forcible manipulations. At the age of 2 years, she had bilateral tibia turnings and later bilateral forcible manipulations. At 2½ years the Achilles tendons were again lengthened on each foot and a bone operation was done in which the head of the astragalus was shifted medial to its original position. This was later followed by another bilateral forcible manipulation. When she was a little over 3 years old she was admitted with stiff rigid feet and she was given 10 months' treatment in plaster casts with wedgings according to the "non-operative" method. Her feet were so rigid little could be done for them. She was released after 10 months with fairly straight feet but these later relapsed. At the age of 6 she returned with relapsed feet (Fig. 12). The head of the astragalus which had been removed at the age of 2 and replaced between the astragalus and scaphoid, slipped out in the soft parts on the dorsum of the foot, and is still living but of no functional value. This roentgenogram shows that at the age of 6 the bones have not fused, even though there is very little

motion in the foot. (Attention is called to this point because there was fusion later.) Cartilage is still present between the astragalus and tibia and between each of the bones of the foot. Non-operative treatment was used for 3 months and then under a general anesthetic the Achilles



Fig. 25. Anteroposterior and lateral roentgenograms before the Achilles tendon lengthening. The forefoot adduction has been corrected and the scaphoid is in front of the astragalus. The posterior end of the os calcis in the lateral view is still drawn up, holding the foot in equinus.



Fig. 26



Fig. 27



Fig. 28

Fig. 26. Lateral roentgenogram after the Achilles tendon lengthening and further wedgings in dorsiflexion, shows that the calcaneus is now at right angle with the tibia. Further dorsiflexion is prevented by bony blocking at the ankle joint. This foot is now ready for club-foot operation.

Fig. 27. Showing feet after the Achilles tendon lengthening and just before operation. Bony blocking prevented

further dorsiflexion. An operation can be done at this time with good prospect of correcting the deformity.

Fig. 28. Feet after operation. The short, thick, extremely deformed feet have been restored to fairly normal looking feet. This can be accomplished best in a 9 year old child by combination of the non-operative and operative methods.

tendon was lengthened, and the posterior capsule divided, and the foot manipulated manually only a moderate amount of force being used. Even with this amount of operative assistance the foot could not be brought up as far as desired. A roentgenogram (Fig. 26) made two weeks after the operation shows some improvement in the position, but that the equinus deformity has not been completely corrected. There is distention of the spaces between the bones, but no fusion of any of the bones. When seen a year later both feet presented solid block of bone (Fig. 27). The patient had had no treatment in the meantime. The equinus deformity had recurred. The fusion of the astragalus to the tibia, or calcus, and cuboid is clearly shown. Clinically the foot is one solid mass of bone, with no motion except in the toes.

I am presenting this case for 3 reasons: first, to show that forcible manipulations and operative procedures may do a great deal more harm to a foot than we realize and should not be used. Second, that when the deformity does recur after forcible manipulations, and bony fusion occurs the feet are very difficult to correct. This foot was later improved by the operative procedure mentioned below. This she should have had instead of the forcible manipulations. The early manipulation and operative treatment robbed this foot of all motion, and there is no operation now that will restore motion to this foot. She walks worse today than the average untreated club-footed patient.

For the past 9 years I have been able to correct 90 per cent of all club-foot cases applying for

treatment, without any form of operative treatment. These children have had no anesthetics, no forcible manipulations, no tenotomies, capsulectomies, decancellation, or bone operations of any kind. The club-feet have been corrected by series of plaster casts and wedgings, according to the principles outlined above. Casts have been applied with the foot held in as much correction as could be obtained, and once or twice a week a wedge shaped portion of the cast has been removed, and the position of the foot changed so as to gain a little more correction, and the cast again closed. After about three such wedgings new casts were applied. The details of this treatment have been described in previous papers so need not be repeated here. At the end of this non-operative treatment the children have feet showing not only excellent anatomical correction, but also flexible feet with almost a normal range of motion. The method requires a long period of time and much effort on the part of the orthopedic surgeon, but the improved results amply repay him for the extra time and effort expended.

G. F., 6 year old boy who had had no treatment (Fig. 29) was given 7 1/2 months of non-operative treatment. The anteroposterior roentgenogram (Fig. 30) shows that the adduction deformity of the forefoot has been cor-

Fig. 29. Non-operative treatment of congenital club-foot, series of cast treatment (Case Smith M.) 30 to 33. The treatment of very special club-foot, study of the results in two hundred cases. J. Am. M. Ass. 1929, 99, 261.





forefoot and ankle. The astragalus points straight downward, almost parallel with the projected midline of the tibia. The adduction of the os calcis points downward instead of up and out forward. No operation should be attempted on these feet until as much of the deformity as possible has been corrected. These feet were treated by casts and wedgings until the adduction and inversion deformities were corrected (Fig. 3). The feet were then brought up in dorsiflexion in order to correct the equinus. The feet showed some improvement when first wedged in dorsiflexion, but after a few weeks showed no further gain in correction (Figs. 4 and 5). An Achilles tendon lengthening was then done on each foot, which allowed the feet to come up a little further. I am always disappointed at the small amount of correction obtained by lengthening the Achilles tendon in congenital club feet, especially when this gain is compared with that obtained in polydactylous club feet. (However if you take advantage of the child being asleep, and forcibly manipulate the feet, you will obtain more correction, but run the risk of getting stiffer feet later.) A roentgenogram after the Achilles tendon lengthening and wedgings in dorsiflexion (Fig. 6) shows that the os calcis which was in equinus has been brought up until it is at right angle with the tibia. It seemed that there was bone blocking which prevented further dorsiflexion. After the maxilloscapular correction was obtained by casts and edgings and Achilles tendon lengthening (Fig. 67) we were justified in resorting to bone operations.

The Hoke club-foot operation was done on each foot, and after 6 weeks in casts "straight last" shoes were applied. Eight weeks after the operations the child was walking and photographs were made (Figs. 68, 69, 70, 71). The feet are normal in appearance, set flat on the floor and give good functional result. The roentgenograms show fusion of the calcaneonavicular, subastragalar, and astragalocalcaneal joints, and the small portion of the head has been replaced, and thus little added to its original position, restoring the feet to fairly normal archi-

ture. There is as free ankle motion as there was before treatment, as nothing has been done to injury the ankle joint. These feet are not as flexible as feet treated early in life by the non-operative method, but are very satisfactory feet.

The best results in older children can be obtained by this combination of the non-operative treatment, and the Hoke club-foot operation.

#### SUMMARY

An analysis has been made of the three types of deformity which go to make up a congenital club-foot. The importance of thoroughly correcting each constituent deformity in turn has been stressed. New emphasis has been placed upon the importance of correcting the inversion deformity before bringing the foot up in dorsiflexion. Failure to do this is responsible for most of the recurrences. A roentgenographic method for the diagnosis of the inversion deformity is described. It is recommended that the feet be corrected by a series of plaster casts and wedgings without the use of an anesthetic and without forcible manipulations or operations. Case reports are given to show the harm of forcible manipulations and the results that can be obtained by the non-operative method. Ninety per cent of the patients can be treated by this method. The Hoke club-foot operation is recommended for the remaining 10 per cent after as much correction as possible has been obtained by casts and edgings.



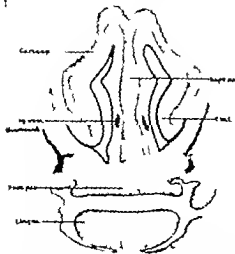


Fig. 4. Diagram drawn from coronal section through nasal area of 60-day embryo. Sept. max., Septum max.—note relative thickness at this stage of development. C. max., concha inferior. Proc. pal., process palatini of maxilla. Org. vom., organum vomeronasale (Jacobson). Cart. cep. max., cartilago cephalica maxilla.

the forty-fifth to the forty-eighth day of embryonic life, and, by their approximation, the anterior portion of the palate is formed, fusing anteriorly with the premaxillary process and posterior to this, with each other (Fig. 4). Fusion has usually taken place between the maxillary and the globular processes by the eighth week and between the horizontal portions of the palate bones by the tenth week (Fig. 5).

The definite causes of failures of union between these various processes are not fully understood, but certainly whatever the underlying etiological factors may be they have marked hereditary tendencies. In this series, the cases with lip or palate, or lip and palate clefts gave positive family histories of such hereditary tendencies in over 54 per cent of cases. These tendencies are shown

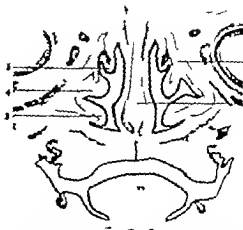


Fig. 5. Diagram of coronal section through nasal area of 65-day embryo. Cartilago cephalica maxilla, septum max., 3, concha anterior, 4, concha media, 5, concha superior. Attention is called to the ossification centers of the vomer.

not only by there being other cases in the family with some type of actual cleft, but also by relatives showing the congenital absence of one or both superior lateral incisor teeth, or by supernumerary superior lateral incisor teeth. In many instances the family history as obtained was not accurate further back than one generation. If detailed family histories for three or four generations could be uniformly obtained I am quite sure the number showing hereditary tendency would be well above the 54 per cent. In numerous cases blood Wassermann tests were made on the parents and on the patients, but syphilis was not found to be an etiological factor in the cleft deformities.

Not infrequently the malformations have been attributed by the parents to maternal impressions, such as fright, extraction of the mother's teeth, or seeing an individual with some facial deformity. In no case, however, has the evidence

Fig. 4. L. L. Age 4½ months. Incomplete unilateral cleft lip. Note complete cleft in the muscle tissue, which causes deviation of nasal septum—swelling of right nostril and flattening of the alar. The skin and mucous membrane are in contact between the margins of the muscle.

Fig. 5. J. M. Age 3 months. Complete unilateral cleft lip and alveolar process. Note the associated lateral deviation of the external nasal structures.

Fig. 6. H. C. Age 4 months. Complete unilateral cleft of lip and palate, showing rotation of premaxilla and typical nasal deformities.

Fig. 7. J. W. Age 6 months. Complete unilateral cleft of lip and palate, showing contour of palate and extreme flattening of alar area.

Fig. 8. M. M. Age 3 months. Note the complete cleft of lip and palate on the left side, incomplete cleft of lip right side.

Fig. 9. M. L. Age 3 months. Bilateral cleft lip. No defects in alveolar process or palate.

Fig. 10. G. H. Age 6 weeks. Bilateral cleft of the lip and of the alveolar process, with anterior rotation of premaxilla. No cleft was present in the horizontal portion of the palate.

Fig. 11. The same patient as in Figure 10, with head tilted back to show the degree of anterior superior rotation of premaxilla.

Fig. 12. A. Z. Age 3 months. Complete bilateral cleft of lip and palate.



Fig 4-



Fig 5



Fig 6



Fig 7



Fig 8



Fig 9



Fig 10



Fig 11



Fig 12

(Legends on opposite page )



Fig. 3

Fig. 3. R. Y. Age, 7 months. Median cleft of lip. Premaxilla absent. N cleft in posterior portion of palate.



Fig. 14

Fig. 14. R. K. Age, 4 months. Median cleft of lip. Premaxilla, philtrum, and nasal cartilage absent. Nasal bones, maxilla, and vomer are rudimentary. Mongolian slant.



Fig. 5

Fig. 5. The same patient as in Figure 14, showing median cleft in lip, the single central nostril, and the well formed palate posterior to the area normally occupied by the premaxilla.

been worthy of scientific consideration as having any possible etiological influence, since in every instance the alleged impressions occurred later than the tenth week of embryonic life, by which time the processes should have been definitely united.

Race does have an important bearing. Clefts of the lip or palate are rare in the negro; there being only 5 cases in this series. It is also of interest to note that we have found these deformities less frequently in Hebrews than in other divisions of the white race.

Figures 4 to 5 show the uncomplicated types of lip and palate clefts, unilateral and bilateral, partial and complete.

In every case of median cleft lip in this series, the premaxilla was absent. The variations in these clefts and in the extent of the associated deformities are shown in Figures 3, 14, 15 and 32.

In submucous clefts of the hard palate there is a deficiency in the bony palate, but the mucosal covering is present. The deficiency may be limited to the posterior portion of the palate or it may be a linear defect extending all the way from the



Fig. 16

Fig. 16. R. T. Age, 7 years. X ray photograph showing submucous cleft in left side of hard palate. Non-erupted unimpacted right canine tooth shown. A cleft in the posterior portion of the soft palate was repaired when the patient was only 4 years old.



Fig. 7

Fig. 7. D. F. Age, 4 months. Congenital transverse cleft of lip.



Fig. 8

right anterior nares. The posterior two-thirds of the nasal fossa was normal.

Fig. 8. D. L. Age, 4 months. Atresia, right nares, coloboma, right eye, nasolacrimal duct absent, cleft lateral cleft lip and alveolar process. Posterior two-thirds of nasal fossa normal.



Fig 19 E C Age, 10 weeks Complete unilateral cleft of lip and palate. Cleft extends into floor of right orbit. Nasolacrimal duct absent. Supra-orbital groove probably due to pressure from amniotic band.



Fig 20 R D Age, 2 months An unusual type of bilateral cleft face. The clefts involve the lips, cheeks, lower eyelids, alveolar processes, anteromedial portions of maxilla, and the orbital floors. Posterior to the premaxilla the palate is intact. Atresia of the posterior one third of the nasal passages was from a thick mass of tissue, partly osseous. Note the rotation of premaxilla and the elevation of all anterior nasal structures, which, in association with the prolapse of the eyeballs, placed the anterior nares and the pupils of the eyes on the same horizontal plane.

posterior margin to the alveolar process (Fig 16). Varying degrees of cleft in the uvula or in the soft palate are sometimes associated with this malformation.

Atresia of the anterior nares (Figs 17 and 18) may be due to organization instead of resorption of the primary epithelial plugs which fill the primitive nasal fossæ, or it is possible that some form

of local pressure may be a factor. Three cases were unilateral, and in each case the obstruction extended to a point approximately at the junction of the anterior and middle thirds of the lower turbinate. The posterior portions of the nasal cavities were normal in each case.

The incidence and cause of atresia of the choanæ (Figs 20 and 31) have been described by Dr J Parsons Schaeffer as follows:

"Should the primitive choanæ just dorsal to the primitive palate not form during the process of development, the epithelial lining of the primitive nasal fossæ and the epithelial lining of the



Fig 21 T H Age, 5 months Complete bilateral cleft lip and palate, showing mucous pits on the lower lip.



Fig 22 L S Age, 5 months Cavernous hemangioma of lower portion of right side of upper lip.



FIG. 1



FIG. 2

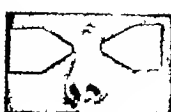


FIG. 3

FIG. 3 A F. Age, 2 1/2 years. Cavernous hemangioma of lips. Telangiectatic type of hemangioma involved greater portion of face, body and extremities.

FIG. 4 C H. Age, 7 years. Lymphangioma of left side of upper lip.

FIG. 5 B J. Age, 7 years. Frontonasal depression probably due to mesangioma. Snout was obliterated before birth.

primitive oral cavity would remain intact, each separated from the other by the thinned-out mesenchymal floor of the early nasal fossae. The continued dorsal growth of the nasal fossae into the mesenchymal mass of the nasofrontal process would ultimately in cases of maximal growth, lead to a condition in which the epithelium of the nasal fossae would come in contact with the epithelium of the foregut, i. e. the nasal portion of the pharynx with a variable amount of mesenchymal tissue between the epithelial surfaces. This would result in blindly-ending definitive nasal fossae dorsally. In other words, an atresia of the choanae or posterior nares. If the amount of mesenchyme between the pharyngeal and nasal epithelia should remain thick, an omocoelous atresia would ultimately be formed.

Absence of the nasolacrimal ducts may be the result of failure of the naso-optic fissure to close (Figs. 19 and 20) or an abnormal closure of the cleft may prevent the formation of the cord of epithelial cells normally formed in the floor of the fissure or a failure in the establishment of a lumen in the epithelial cord (Fig. 18).

Colobomas result from the incomplete closure of the embryonic choroidal fissure, and may be limited to the iris and choroid, or may extend into the eyelids or even into the facial clefts. Three types in which the facial clefts are involved are shown in Figures 18, 19, and 20.

Congenital mucous pits in the lower lip are all symmetrically placed one on each side, approximately in front of the lateral incisor teeth (Fig. 1). It is not clearly understood how they can have any direct relation to the embryonic clefts, yet when present they are usually associated with bilateral cleft lip. In a few cases there were no lip clefts but cleft palate existed. In three instances pits were present without lip or palate clefts, but in each of these cases the individuals were from families in which, for three or four generations, cleft lips and palates had occurred frequently. Our 14 cases were from 3 family groups, in which this malformation occurred in 5, 5 and 8 individuals, respectively. Sir Arthur Keith, who has studied this subject, finds that the nearest explanation he can give for the occurrence of such pits is that they may be a possible reversion to the mucous glands which are normally found in the lip of the shark.

Hemangiomas may be the telangiectatic form or the cavernous form. Since they are found in the region of the angles or fissures about the face and neck they have been thought to be congenital displacements. Figures 22 and 23 illustrate two types of lip involvement.

Lymphangiomas are tumors analogous to hemangiomas except that they are composed of spaces and channels containing lymph instead of blood. They may be telangiectatic, cavernous, or



Fig 26 A. G. Z. Age, 8 months Microtia, atresia external auditory canal, and unilateral cleft lip



Fig 27 A. Z. Age, 11 years Macrotia and marked prolapse of auricle

leading to the cysts which apparently had their origin from the area overlying the frontonasal suture Each cyst contained hair and sebaceous material

cystic The case shown in Figure 24 was of the cavernous type

The two cases of dermoid cysts of the dorsum nasi had had unsuccessful attempts at removal Each presented a fistulous tract with its opening just above the lower ends of the nasal bones and

The frontonasal depression shown in Figure 25, I believe was due to a meningocele which was obliterated before birth In the correction of this deformity a cartilage transplant was used to fill up the depression In making the bed for the transplant the periosteum was loosened from an area about the frontonasal suture The bone was



Fig 28 Fthmocephalus with cyclopia and other associated deformities Lived only a few minutes



Fig 29 Profile of the monstrosity as shown in Figure 28 Note the position of the snout like nasal appendage.





Fig. 30



Fig. 31



Fig. 32

Fig. 30 B. P. lived hours. Exenoccephalus with anophthalmia. Snout like nasal appendage was patent. Rudimentary orbits were lined with conjunctiva, but eye balls were absent.

Fig. 31 M. H. Age, 8 months. Anophthalmos and com-

mon stream of choroid. Note groove in dorsum and separating the anterior nerves.

Fig. 32 B. S. Age, 6 hours. Hemicephalus, median cleft lip. Premaxilla absent and rudimentary nasal bones. Spina bifida in lumbar area.

not disturbed, yet for 8 days cerebrospinal fluid escaped through the skin incision. No complications arose and in all other respects the convalescence was uneventful. X ray plates made before operation did not show an appreciable opening in the suture line.

Microtia and atresia of the external auditory canal are usually associated. The external ear develops from the first branchial groove and its adjoining tissue. The auricle arises from six elevations, three of which appear on the mandibular and three on the hyoid arch. The external auditory meatus develops as an ingrowth of the first branchial groove. Malformations of the middle ear are sometimes present, as well as malformations arising from more distant portions of the first or second branchial arches, such as clefts in lip or palate (Fig. 36).

In macrotia the deformity is usually exaggerated by obliteration of the antihelix fold and varying degrees of prolapse (Fig. 37).

Rudimentary mandible and micrognathia were found in cases. In a third case these deformities were present in addition to a cleft of the palate to the premaxilla. All cases had great difficulty with respiration and deglutition and died within 3 or 4 days after birth.

Cyclops results from an abnormal development of the anterior portion of the brain and faulty separation of the optic vesicles. The monstrosity shown in Figures 28 and 29 lived only a few minutes. The large central eyeball with a

single large pupil lies in the region of the root of the nose. The snout-like appendage or proboscis is placed above it. The skeleton of the anterior and upper part of the face is defective. The maxillary processes have fused solidly across the midline. Coronal sections were made through this head by Dr. J. Parsons Schaeffer who has as yet not published his studies on the specimen, but very kindly sent me the following note on the type of formation.

When the nasal bones fail to form, save possibly far forward in the roof of the mouth over the premaxilla, or as small and short tubular, blindly-ending canals, as in cyclopaean monsters, the frontonasal process fails to be partitioned, and what ordinarily thins down to become the nasal septum remains a thick, heavy bar bounding the roof of the mouth. In these cases, despite the fact that it is not necessary for the palate to form to separate the mouth cavity from the nasal fossae, since no nasal fossae exist, the dorsal parts of the premaxilla of the palatal shelves have the potency to develop, and indeed do develop into the soft palate and voile. Thus the hind part of the mouth cavity comes to be overlaid by a space over the soft palate, which space is in direct continuity with the nasal pharynx and is a large measure part of it. In the absence of the nasal bones proper the space has no connection with the anterior nares, should they be formed. Usually the soft palate in these cases is normal in thickness and in its relation to the structures contained in the nasal pharynx. A puncture through the soft palate would open into the space above the dorsal and superior part of the mouth cavity. In the absence of nasal bones, it is obvious, however, that little could be accomplished by such puncture in these defective cases. It should, of course, be understood that the above statement applies only to those types of nasal streamers in which, for all practical purposes, the nasal bones are absent.

Ethmocephalus with anophthalmia is shown in Figure 30. In some respects the malformations closely resemble those presented in Figure 28. In this case, however, there were two rudimentary orbits with conjunctival lining, but no eyeballs. The child lived for 2 hours, and although the opening in the snout-like appendage (which had no bony framework) was quite small, it was patulous as evidenced by the bursting of small bubbles of mucus at the opening by the expired air.

Fortunately anophthalmia occurs most frequently in non-viable monsters. The etiology is uncertain but sometimes has been regarded as a complication of hydrocephalus. The patient shown in Figure 31 is now 5 years old, shows evidence of arrested hydrocephalus, is definitely idiotic, and exceedingly ill tempered. Another unusual deformity in the case is the groove, in the lower portion of the dorsum nasi, which separates the nasal cavities.

A case of hemicephalus, median cleft lip, absent premaxilla, rudimentary nasal bones, spina bifida, is shown in Figure 32. Whether the arrested development in this monstrosity was due to some primary defects in the germ cells, or to causes acting upon it from without—such as amniotic deformities—is uncertain. The ape-like appearance is most striking and suggests atavism. This child lived 6 hours.

A case showing congenital temporomandibular fibrous ankylosis, with incomplete fusion of the mandibular and maxillary gingival margins (Fig. 33), presented interesting problems as to etiology. Since this case is to be reported in detail later, by Dr. Norman M. MacNeill, it is only mentioned here as one of the deformities found in this group of cases.

The wide range in the types of facial malformations found in this series has interested us not



Fig. 33. E. K. Age 3 months. Incomplete fusion of the mandibular and maxillary gingival margins.

only in the embryological considerations, but also in the surgical problems encountered in their repair. A paper dealing with the operative measures and the results obtained will be presented later.

#### REFERENCES

1. BIRNBAUM, R. *Malformations of the Fetus*. Philadelphia: P. Blakiston's Son & Co., 1912.
2. BLAIR, VILRAY PAPIN. *Surgery and Diseases of the Mouth and Jaws*. St. Louis: C. V. Mosby Co., 1918.
3. DAVIS, WARREN B. *Development and Anatomy of the Nasal Accessory Sinuses in Man*. Philadelphia: W. B. Saunders Co., 1914.
4. Idem. Development of the bones of the face. *Internat. J. Orthodontia*, 1917, 3, No. 10.
5. Idem. Harelip and cleft palate—a study of four hundred and twenty five consecutive cases. *Ann. Surg.*, 1928, 87, 536.
6. MACCALLUM, W. G. *A Text Book of Pathology*. Philadelphia: W. B. Saunders Co., 1928.
7. PRENTISS, C. W., and AREY, L. B. *Text Book of Embryology*. Philadelphia: W. B. Saunders Co., 1920.
8. SCHAEFFER, J. PARSONS. *The Nose and Olfactory Organ*. Philadelphia: P. Blakiston's Son & Co., 1920.
9. Idem. Atresia of the choanae: its incidence and cause. *Laryngoscope*, 1933, June.

## FOREIGN BODIES IN THE STOMACH

## REMOVAL BY PERORAL ENDOSCOPY

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THE removal of esophageal foreign bodies by esophagoscopy is now generally accepted as the only plan of treatment worthy of consideration. There are however sporadic attempts at removal with the aid of the probing, bougie, stomach tube and other unsafe and unscientific measures. No one plan of treatment of foreign bodies in the stomach has been generally accepted. Removal by peroral gastroscopy would seem to be the safest method. Surgery has its advocates while blind methods commonly aided by a single plane fluoroscope also are practiced.

Experience has shown that a majority of foreign bodies entering the stomach spontaneously will also pass spontaneously through the pylorus. Exceptions are noted in large objects and in cases of pyloric stenosis. More important than this, however, is the question whether the foreign body having passed through the pylorus will be able to pass safely through the intestinal canal. Long foreign bodies as small pins, nails, hairpins, bob-bette pins and sharp objects as needles, long pins and safety pins are often unable to negotiate the turns in the intestines, notably the duodeno-jejunal junction. The question therefore arises, should we remove the foreign body while it still remains in the stomach or allow it to remain, keeping it under observation and removing it only if it becomes lodged in the intestines? If removal from the stomach is contemplated what are the criteria to be considered in arriving at such a conclusion and what method of removal should one employ?

The mere presence of a foreign body in the stomach is no indication for its immediate removal. During a 10 year period ending January,

1934, 849 cases of radio-opaque foreign bodies in the stomach and intestinal canal were admitted to the Bronchoscopic Clinic at the Jefferson Hospital. Of these 58 passed spontaneously, 22 were removed from the intestinal canal by laparotomy, one was removed from the sigmoid by peroral endoscopy and 8 were removed from the stomach by peroral gastroscopy. In the group that passed spontaneously there were many open safety pins, common pins, large corns and dials, dentures, toys, and other pointed or irregular foreign bodies. It must therefore be admitted that the number of objects failing to pass is rela-

tively small and that there should be definite indications for mechanical removal.

The dangers of injury to the stomach by a swallowed foreign body are remote. Exceptions to this are noted in cases of insane persons and others swallowing large numbers of objects which become entangled forming a matted mass and in cases of swallowing certain agents, as radium. Single foreign bodies have been known to remain in the stomach for long periods without harmful effects. Jackson reported the case of a tooth paste cap remaining about 3 years in the stomach of a patient with pyloric stenosis. Myerson reported cases of long duration.

The opinion of the experienced roentgenologist is the only safe guide in determining if a given foreign body will be able to leave the stomach and pass safely through the intestines. The latter is important for removal of a foreign body from the stomach is more readily and safely performed than removal from the duodenum. This should be further emphasized when one recalls that a majority of the patients in whom surgical removal is required are young children. Eight of Shallow's cases were 4 years or less in age and of these 4 were under 1 year. In 6 the foreign body was removed from the duodenum.

The criteria then are, first, comparative roentgenographic studies of the maximum diameter of the foreign body to determine if it will pass through the pylorus (Fig. 1); second, similar studies of the length of the object as well as its lesser diameter to ascertain if it will be able to traverse the angulations of the intestinal tract (Fig. 2). This phase of the subject has been thoroughly discussed by Mingos, who with his associates, has had an enormous experience with alimentary canal foreign bodies.

If in the opinion of the roentgenologist the foreign body is deemed to be too large or too long to pass, removal should be proceeded with. In the case of a large foreign body as a disc or coin which cannot pass the pylorus there is no need for haste. In the case of a long or pointed object, as needle, long pin, bob-bette pin, or hair pin removal should be prompt lest it leave the stomach and lodge in the duodenum.

The method of removal must now be considered. The accessibility of the stomach to surgical



Fig 1 Roentgenogram made in the case of a child, aged 3 years, exhibiting a loose leaf ring in the stomach (Case 11). The ring had been swallowed 11 days previously. Owing to its large size and shape, it was the opinion of the roentgenologist that the foreign body would not leave the stomach spontaneously and should be removed. This type of foreign body, being freely movable and devoid of sharp points or edges could remain indefinitely in the stomach with safety. (Film by Dr J T Farrell, Jr)

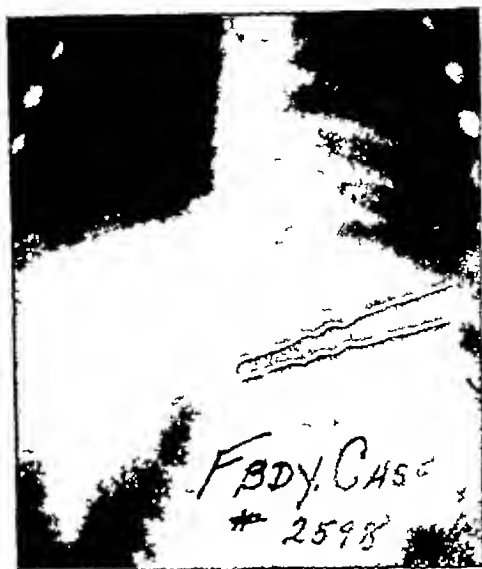


Fig 2 The hairpin which entered the stomach spontaneously remained in practically a fixed position during its brief sojourn (Case 9). Although properly directed with the closed end toward the pylorus its length very probably would have interfered with making the turns in the duodenum. Prompt removal was recommended. (Film by W F Manges)

exploration is commonly the determining factor in deciding on gastrotomy. To the surgeon inexperienced in this field, penetrating the stomach wall or opening that viscus introduces a very definite element of danger. In Myerson's report, surgeons performed gastrotomy on 5 of his cases. In 3, the foreign body was found and removed, in 2 the operation proved to be unnecessary as the foreign body had already left the stomach. There was 1 death 3 days after operation. In addition, these cases must be hospitalized for about 10 days. The method of choice which obviates these dangers and objections consists of removal of the foreign body by the route which it took when entering the stomach, namely, peroral gastroscopy.

*Peroral gastroscopic removal of foreign bodies*, without general anesthesia, aided by a roentgenologist using a double plane roentgenoscope has been successfully performed in a number of cases. Dangers of infection of the peritoneal cavity are non-existent. Hospitalization for 1 or 2 days is usually necessary. This work should be performed only by one experienced in gastroscopy, aided by a roentgenologist familiar with the technical phases of double plane roentgenoscopy. This is often a serious drawback as operators experienced and properly equipped are not always available.

Of the 18 cases of gastroscopic removal 12 were removed by the writer (Fig 3). The table gives the ages of the patients, the length of sojourn of the foreign bodies in the stomach, and the duration of the convalescence following gastroscopy.

These data together with the character and size of the objects removed set forth some of the

Case	Foreign body number	Age	Foreign body	Length of sojourn in stomach	Sojourn in hospital after removal of foreign body
1	1422 C	8 mos	Open safety pin	6 days	Not admitted
2	1712 C	13 yrs	2 capsules containing 100 mgm radium	3 hours	1 day
3	1964 C	2 yrs	Penny	40 days	1 day
4	2036-C	1 yr	Open safety pin	2 days	3 days
5	2086-C	3 yrs	Hairpin	2 days	3 days
6	2358-C	3 yrs	Nail	1 day	1 day
7	2517 C	8 mos	Open safety pin	1 day	2 days
8	2586-C	2 1/2 mos	Open safety pin	3 hours	1 day
9	2593-C	15 mos	Hairpin	4 hours	1 day
10	2731 C	2 yrs., 8 mos	Bobette pin	20 days	1 day
11	809-C	3 yrs	Loose leaf ring	11 days	1 day
12	967 C	11 mos	Open safety pin	3 days	2 days

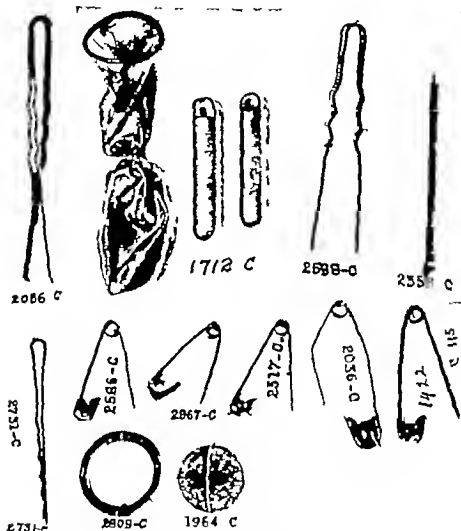


Fig. 3. A photographic reproduction (actual size) of gastric foreign bodies removed by peroral gastroscopy with roentgenoscopic assistance using double plane fluoroscope. The foreign body number of each object corresponds with the number given in the accompanying table.

indications for removal and also emphasize the advantages of this method. In all of these it was the opinion of the roentgenologist that the foreign body would not pass spontaneously and that mechanical removal should be resorted to.

In all of these the foreign bodies were removed by fluoroscopic gastroscopy. In the older children a preliminary sedative was given hypodermatically. Neither local nor general anesthesia was employed. The length of sojourn in the hospital after removal of the foreign body was from 1 to 3

days, the average being  $\frac{1}{2}$  days. In Case 1 the patient was not admitted.

The radium capsules (Case 2) containing 100 milligrams of radium element could have passed spontaneously. This would have required 48 to 72 hours, but would have resulted in serious injury. They were removed within 1 hour after the loss was detected. The prolonged sojourn of the penny in the stomach (Case 3) was apparently due to stenosis of the pylorus. No reason could be ascribed to the failure of the bobette

pin (Case 10) to leave the stomach within 29 days. Foreign bodies of this type commonly leave the stomach promptly although they may lodge at the duodenojejunal junction.

The views formerly held that foreign bodies in the stomach should be observed for a time before proceeding with removal have been modified to the extent that a decision is now made when the patient first comes under observation. If it is the opinion that the foreign body will not pass, peroral gastroscopy is promptly proceeded with. If it is believed that the object can pass, the patient is observed fluoroscopically and is continued on its regular diet. If the foreign body fails to leave the stomach within a reasonable time removal is carried out. In Case 1, the safety pin was observed for 5 consecutive days before deciding to remove it. A "reasonable time" depends on the character of the foreign body. A coin might remain indefinitely in the stomach without harmful results, whereas a needle should be removed without delay.

#### CONCLUSIONS

A majority of swallowed foreign bodies will pass spontaneously if undisturbed. In questionable cases the opinion of a competent roentgenolo-

gist should be secured to determine if the object can leave the stomach and also if it will be able to traverse the angulations of the intestinal canal, particularly the duodenojejunal junction.

In all cases where it is believed that the foreign body cannot pass removal should be carried out.

The safest and best method of removal of a swallowed foreign body from the stomach is by peroral gastroscopy with roentgenoscopic assistance using a double plane roentgenoscope.

#### REFERENCES

- 1 CLERF, L. H. Radium capsules in stomach, gastroscopic removal. *Am J Roentgenol*, 1927, 17, 635.
- 2 Idem. Foreign bodies in the gastro-intestinal tract. *Surg Clin N America*, 1934, 14, 77.
- 3 JACKSON, C., and SPENCER, W. H. Safety pins in the stomach, peroral gastroscopic removal without anesthesia. *J Am M Ass*, 1921, 76, 577.
- 4 MANGES, W. F. The roentgenology of foreign bodies in the esophagus and gastro-intestinal tract. *Surg Clin N America*, 1934, 14, 89.
- 5 Idem. Foreign body removal with the aid of the double plane roentgenoscope. *Am J Roentgenol*, 1933, 30, 674.
- 6 MYERSON, M. C. Foreign bodies in the stomach and intestines. *Trs Am Laryngol. Ass.*, 1932, 50, 41.
- 7 SHALLOW, T. A. The treatment of foreign bodies in the gastro-intestinal tract from the surgeon's viewpoint. *Surg Clin N America*, 1934, 14, 57.

## THROMBO-ANGIITIS OBLITERANS (BUERGER) VI

## TREATMENT OF 524 CASES BY REPEATED INTRAVENOUS INJECTIONS OF HYPERTONIC SALT SOLUTION: EXPERIENCE OF TEN YEARS

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THE results obtained in the treatment of patients suffering with thrombo-angiitis obliterans by repeated intravenous injections of hypertonic salt solution can now be surveyed from an experience of 10 years. This method of treatment was introduced by the writer in 1923 and a preliminary report was published in 1926, tentative conclusions being drawn from the results obtained in 66 patients (7). By 1930 the number of patients treated had increased to 289, and a more accurate estimate of the value of the method was then presented (8). The series now includes 524 cases, and the results previously reported have been consistently duplicated and improved. This summary gives a true picture of what this form of treatment may accomplish.

The experience gained from the observation and treatment of this group of patients has justified the conclusion that thrombo-angiitis obliterans is not necessarily the terrible mutilating disease it is popularly thought to be. By applying the knowledge we already have the disease can be arrested; amputations can be avoided; patients can be restored to good health and recurrence of trouble can be prevented. Failures in treatment are practically always limited to those cases in which the condition is not recognized early enough and individuals are first seen in a hopelessly advanced state of the disease or the patients refuse to co-operate completely in their treatment.

## CLINICAL MATERIAL

Of the 524 patients who are included in this report, 249 were treated in the special clinic for thrombo-angiitis obliterans in the Out Patient Department of The Mount Sinai Hospital, and 275 were treated by the writer in his private practice. The method of treatment was the same in both groups. Every patient treated for 1 month or longer is included. In other words, if a patient was discouraged by a lack of improvement after 5 or 6 weeks of treatment and was treated elsewhere with an unfavorable outcome, such a patient is listed as unimproved. If a patient was not benefited by treatment under my care, but obtained more favorable results by treatment elsewhere, he is likewise included as unimproved.

The cases are divided into two groups, and the figures are given separately for each. In the first group, classified as typical thrombo-angiitis obliterans, are included patients who gave clear-cut symptoms of arterial disease before the age of 45 years. From this group are excluded young individuals with arterial disease due to infections or toxic agents, and instances of preexisting arteriosclerosis associated with diabetes and other metabolic disorders. The second group, labeled border-line thrombo-angiitis obliterans, includes patients with organic arterial disease in which onset of symptoms was between the ages of 45 and 55 years. Great care was exercised to exclude from this group all patients who appeared to be suffering from early arteriosclerosis. When the first symptoms of impaired circulation appeared after the age of 55 the diagnosis of arteriosclerosis was made and such patients are not included in this summary.

A patient with vascular disease in the extremities, who first develops symptoms in the feet, may be suffering from early arteriosclerosis or a late onset of thrombo-angiitis obliterans. The differentiation of these two conditions is important as the prognosis is not the same in both. Thrombo-angiitis obliterans is an inflammatory condition. Its etiological cause is known and can be eliminated, bringing the progression of the disease to a halt. The outlook in this condition is relatively good. On the other hand, arteriosclerosis is a degenerative lesion, part of the natural aging process, and permanent arrest is not possible. Under treatment, some temporary improvement can usually be obtained or the advancement of the condition may be retarded, but this benefit is gradually lost with the inevitable progression of the disease. The criteria used for differentiation of the two conditions are summarized in Table I. It must be understood that one of these factors alone suffices for differentiation, but the combination of many features makes up a clinical picture that is fairly recognizable.

## METHOD OF TREATMENT

The solution used is 5 per cent sodium chloride. It is prepared in freshly distilled water filtered,

TABLE I—CRITERIA FOR DIFFERENTIATION BETWEEN THROMBO-ANGIITIS OBLITERANS AND ARTERIOSCLEROSIS IN PATIENTS BETWEEN FORTY AND FIFTY YEARS OF AGE

Thrombo-angitis obliterans	Arteriosclerosis
Appears younger than his age	Appears older than his age
Hair normally pigmented	Hair usually gray
No arcus senilis	Arcus senilis frequently present
Retinal arteries normal	Retinal arteries usually sclerotic
Blood pressure usually low	Blood pressure often high
Radial and temporal vessels soft	Radial and temporal vessels thickened and hard
Upper extremities frequently involved	Upper extremities seldom involved
Femoral arteries frequently closed	Femoral arteries seldom closed
No calcification of vessels on x ray	Calcification of vessels on x ray frequently seen
Blood volume usually diminished	Blood volume usually normal
Symptoms of coronary artery sclerosis rare	Symptoms of coronary artery sclerosis frequent
Aorta appears normal on x ray	Aorta sometimes appears elongated on x ray
Albuminuria rare	Albuminuria not uncommon
History of migrating phlebitis frequent	History of migrating phlebitis rare

and immediately sterilized. Since bacteria grow rapidly in distilled water, immediate sterilization is important to avoid contamination. If injections are followed by chills or temperature reaction, the cause is almost always found in failure to follow this rule.

Injectations are given by the gravity method into a superficial vein at the elbow. Occasionally when the arm veins are very small, the external jugular vein is employed. The initial dose is 150 cubic centimeters and all subsequent injections are 300 cubic centimeters. The fluid is allowed to run in slowly, about 10 minutes usually being required for the injection. During this time patients are kept lying flat. While the treatments are being given, patients become very thirsty and many of them experience a sensation of warmth. They are allowed to get up as soon as the injections are finished and may return to work. One of the great advantages of this method of treatment is that it is ambulatory and it does not interfere with employment. The injections are at first given on alternate days three times a week, later twice a week, and the length of intervals is further increased as the patients improve. The total duration of treatment varies from 6 weeks to 2 years, depending upon the severity of the individual case. Patients are discharged when all symptoms have disappeared or when the maximum possible improvement has been obtained.

#### ROLE OF TOBACCO

Again, as in previous papers, the importance of tobacco as the exciting cause of thrombo-angitis obliterans must be stressed. The evidence in support of this contention is overwhelm-



Fig. 1 Two views of leg showing enormous size of ulcer healed by author's methods

ing. In over a thousand instances of thrombo-angitis obliterans studied by the writer, a typical case of this disease in a non-smoker has never been seen. Cessation of smoking regularly results in arresting the disease, while continued use of tobacco is coincident with further progression. In innumerable instances, patients who have been restored to good condition by treatment and elimination of tobacco have shown recurrence of trouble when they resumed smoking. In practically all cases of relapse with ulcer formation, gangrene, or amputations, patients have admitted returning to the use of tobacco. In several early cases of thrombo-angitis obliterans, cessation of smoking without any treatment whatsoever, has resulted in complete disappearance of all symptoms. This regular association of the use of tobacco with the occurrence and the progression of the disease is too striking to be ignored. Although a constitutional susceptibility to tobacco must be assumed, the rôle of this agent as the exciting cause cannot be doubted.

How is one to reply to those who claim to have seen instances of thrombo-angitis obliterans in non-smokers? One can only be skeptical of the accuracy of the diagnosis. There is no pathognomonic clinical or laboratory sign by which thrombo-angitis obliterans can be recognized. While perfectly typical examples of the disease are readily identified, less characteristic cases must be differentiated from presenile arteriosclerosis and arteritis which are due to other causes such as syphilis, rheumatic fever, and toxins of



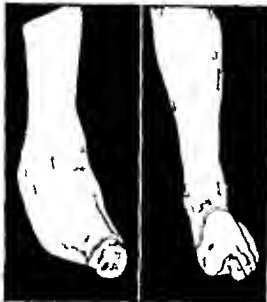


Fig. 2 Photographs showing feet healed by author's methods. Note extensive involvement in both cases. Black line indicates area of anesthesia still present following nerve section. Note primary healing of operative wounds on legs.



Fig. 3 Photograph showing healed feet after extensive involvement with loss of toes. Treated by author's method.

various kinds. In such instances the diagnosis of thrombo-angitis obliterans must be made by exclusion, and the possibilities of error are great. In order to establish that thrombo-angitis obliterans can occur in a non-smoker, the case must be perfectly typical. The writer has never seen such an instance.

The importance of recognizing the relationship between the use of tobacco and the development of thrombo-angitis obliterans is far from academic. In order to treat patients with this disease successfully they must be made to stop smoking. It is frequently difficult to induce patients to accept this restriction, but no compromise can be made on this point. Cessation of the use of tobacco is the most important part of the treatment, as this stops the progression of the disease. Efforts to improve the collateral circulation by the repeated injections of hypertonic salt solution are secondary.

#### IMPORTANCE OF FOLLOW UP

Before presenting any data showing the results obtained it is necessary to stress the importance of a long and careful follow-up of treated patients. Thrombo-angitis obliterans is a chronic disease, subject to periods of spontaneous remission. A

fair percentage of favorable results may therefore appear to follow any method of treatment, if the period of observation is short. Freedom from recurrence for several years is looked upon as essential in establishing the cure of malignant disease, and a similar safeguard is necessary in judging the cure of thrombo-angitis obliterans. A persistent effort has been made to keep in touch with all patients in our treated group, and frequent re-examinations have been made as the years have gone by. Table II presents a summary of the period of follow-up. Of 450 living and unamputated cases 396, or 86 per cent, have been followed from 1 to 10 years. Of this group 313, or 69 per cent, were last examined in 1933 or 1934.

The impression prevails that thrombo-angitis obliterans is a progressive disease inevitably leading to gangrene and amputation of extremities. In part this belief has resulted from observations of patients who had this disease 20 years ago, and whose clinical course was characterized by successive amputations. In part the belief has been fostered by statements made in recent articles, such as "the disease usually progresses slowly and may remain temporarily quiescent in any one of the earlier stages" (1) and "we perform bilateral sympathectomy even though the disease appears to produce symptoms in only one extremity since ultimately it is almost sure to involve the opposite extremity" (2).

The experience gained from following the course of individuals treated during the past 10 years does not support the statement that thrombo-angitis obliterans is a progressive dis-

TABLE II—FOLLOW-UP RESULTS IN 524 CASES OF THROMBO-ANGITIS OBLITERANS

Period followed in years	Cases	Dead or not stated	Living and stated	Credit given when living
Less than 1	65	21	44	17
1	52	12		40
2	50	13	37	34
3	52	6	46	3
4	47	6	41	35
5	42	3	39	27
6	2	1	1	1
7	31	3	28	2
8	1	0	11	21
9		0	0	0
10	5	0	5	5
Total	524	62	462	181

50% or less per cent of living cases stated to be cured. 10% or less per cent of those followed for 10 years.

case provided the patients have discontinued using tobacco. Three hundred and nine patients with this ailment who have stopped smoking and have been restored to good condition by treatment, have been repeatedly examined during a period from 2 to 10 years after treatment was first started. Not a single amputation has been necessary in this entire group. The vast majority of these patients have had no treatment for years. They have returned to active employment and are engaging in all normal activities without any recurrence of trouble in the extremities.

Rarely a case appears to show progression. In 4 of the 300 cases in this group, thrombosis of a previously open popliteal artery has been observed although the patients denied smoking. While it is difficult to prove that such occurrences do not mean actual progression in these few cases, another explanation may be entertained. It is possible that, during the time the disease was still active, the walls of these popliteal vessels were damaged. A localized proliferation of the intima at such a site might in time be responsible for a piling up of platelets, and the gradual formation of a mural thrombus, which eventually would occlude the lumen completely. The fact that gangrene of the feet did not develop in any of the cases in which such occlusion took place suggests that the process was slow and that collateral circulation developed as the main vessel gradually became obstructed. The experience cited justifies the conclusion that thrombo-angitis obliterans is rarely progressive in a patient who has stopped smoking.

TABLE III—RESULTS OF TREATMENT IN 524 CASES OF THROMBO-ANGITIS OBLITERANS

	Cases	Amputated	Unamputated	Amputated	Deceased
Typical thrombo-angitis obliterans	435	353	0	36	14
Excluded cases	89	0	13	4	10
Total	524	353	13	40	24

Percentage of amputations required, 76 per cent.

### AMPUTATIONS

The percentage of amputations required serves as the best single criterion of the success or failure of a method of treatment for thrombo-angitis obliterans. Unclipped and untreated cases of this disease go on to amputation in the vast majority of cases. In a study of 460 cases published in 1930 (5), it was shown that 64 per cent of all such untreated cases had suffered amputation of at least one extremity in the first 5 years of the disease. A striking reduction in the percentage of amputations necessary may be regarded as evidence of the merit of a given method of treatment.

Forty amputations (7.6 per cent) have been performed among the 524 treated cases which form the basis of this report. This includes all amputations done, no matter where and by whom. If patients were temporarily benefited but subsequently relapsed and required amputation, they are included as failures of the treatment. To assume that amputations done in other institutions might have been avoided if the patients had remained under our care is not justifiable. Unless all treated patients are carefully traced, many such amputations will not be recorded. Thus no statement of the percentage of amputations required is reliable unless it is accompanied by a corresponding statement of the percentage of accurate follow up of treated patients. Only in this way can the probable error be estimated. The reader is again referred to Table II which shows that 86 per cent of our cases were followed from 1 to 10 years.

Comparative statistics from other clinics are unsatisfactory because exact follow-up figures are not given. The following statement of the results obtained at the Mayo Clinic is quoted in spite of this discrepancy: "Statistics for 1928 to 1932 inclusive disclose an incidence of major amputations, at the clinic, of 13.8 per cent of all patients suffering with Buerger's disease, and subsequent major amputations of 7.5 per cent, making a total incidence of amputations of 21.3 per cent" (3). In his recent monograph on thrombo-angitis

TABLE IV.—STUDY OF LEVEL OF AMPUTATIONS (BY YEARS)

Year	No. cases	By no.	Below knee	Below knee	By others	Above knee	Above knee	Conservative	Amputation
1901									
1904									
1905									
1906				3					
1907									
1908	7				6	1			
1909	7								
1910									
1911									
1912	6							3	
1913									
1914									
Total	40	9	3	16	16	4	19	3	

\*One forearm amputation.

obliterans, Drex states that he had 1.8 per cent failures in 119 cases treated by ganglionectomy. (4) These figures may be compared with 7.6 per cent, the percentage of amputations required where patients were treated with injections of hypertonic salt solution.

A more detailed study of the number of amputations required gives information of value. Since cessation of smoking is included as part of this method of treatment, the amputations performed have been divided into those who co-operated in this respect and those who did not (Table V). It is at once apparent that about 50 per cent of the patients who required amputation persisted in smoking in spite of repeated warnings to stop. This striking fact is part of the evidence that the use of tobacco is the essential active cause of thrombo-angitis obliterans.

Table V is also subdivided into first and second amputations. Patients who present themselves for treatment because of symptoms in a second extremity after one has already been amputated, are obviously advanced cases of the disease. Four hundred and forty-nine patients were first seen before an amputation was performed. Sixteen of these patients, in spite of good co-operation in discontinuing the use of tobacco, nevertheless required amputation. This figure represents 3.5 per cent of the total number in this group. Several of these patients presented extensive gangrene of the foot on first examination, and treatment was given to make possible a low amputation. However in an unselected group of patients with

thrombo-angitis obliterans, this figure (3.5 per cent) may be accepted as indicating the percent age of patients in whom amputation is probably unavoidable.

The necessity for amputation of an extremity arises from massed gangrene, which makes the saving of a useful foot impossible, or from spreading infection which threatens life. Relief of severe pain can now be so completely accomplished by the simple operation of peripheral nerve section, that this cause no longer needs emphasis. The trend toward conservatism has been greatly aided by this valuable addition to our therapeutic aids, which will be referred to again.

Massive gangrene is an indication for amputation when it is so extensive that a useful foot can no longer be saved, or when the patient's general health is being so undermined by absorption from the necrotic foot that life itself is threatened. It requires discriminative judgment to decide in which instance a conservative policy may be followed and in which a more radical course is wiser. It is unjustifiable to lose a patient's life in an attempt to carry conservation to an extreme.

The other serious complication which occasionally defeats conservative efforts and demands amputation is spreading infection. When one considers how often ulceration of the toes and feet occur in thrombo-angitis obliterans, and that poor nutrition of the tissues interferes with resistance to infection it is surprising that severe spreading infection is not encountered more often. On the contrary individuals with thrombo-angitis obliterans are strikingly resistant to infection. Localized infections associated with moderate temperature can be treated conservatively with incision and wet dressings, and in most cases will subside. In rare instances infection spreads rapidly along tendon sheaths, and in spite of wide incision and drainage, advances so rapidly as to threaten life. Under such circumstances, the only course to follow is high amputation. Table IV includes 3 such cases.

Finally a word should be said about the level of amputation. In the paper published in 1930 (8) it was pointed out that when amputation became necessary in cases treated by this method, the limb could be removed below the knee in practically all cases. The importance of saving the knee joint cannot be overestimated. With an amputation below the knee an artificial leg can be used without the aid of a cane, and the gait is so natural that the patient does not appear to be crippled. This fact is of paramount importance when the patient again seeks employment, as obviously crippled men have great difficulty in

TABLE V—ANALYSIS OF AMPUTATIONS REQUIRED IN DIFFERENT GROUPS OF PATIENTS WITH THROMBO-ANGIITIS OBLITERANS

	Total cases	Total amputations	Continued smoking	Stopped smoking
Early cases with no amputations when first seen	449	28	12	16
Advanced cases with one or more amputations when first seen	75	12	7	5
Totals	524	40	19	21

finding positions. Of the 40 amputations reported, 19 were performed by me or at my direction, and 16 of these were successfully done below the knee (Table IV). Of the 20 lower extremity amputations listed as done by others, only 4 were performed below the knee.

#### ADDITIONAL METHODS OF TREATMENT EMPLOYED IN THE HEALING OF ULCERS

Ulceration of the toes or foot was present in 255 of the 524 treated cases (Table VI). Of these 174 are healed. The remaining 81 are divided as follows: 42 patients who had amputations or have died, 23 who discontinued treatment, and 16 who have been treated only a short while. Excluding those who required amputation, all but 3 patients who remained under my care for more than a year have been completely healed.

While all of these patients received routine injections of hypertonic saline solution, certain additional measures were employed. All patients with ulcers were advised to rest as much as possible with the extremity in a horizontal position. They were supplied with crutches so that weight bearing on the affected foot could be avoided. The local treatment in most cases consisted simply of cleansing with ether and applying desitin ointment.<sup>1</sup> If there was added infection, immersion of the affected part in Carrel-Dakin solution was occasionally used. In flat wounds which showed healthy granulation, strapping across the surface with adhesive strips often proved useful.

The relief of pain caused by ulceration of the extremities presents a special problem. Not only is there a great deal of spontaneous pain in the wound, but the dressing of the exceedingly sensitive ulcerated area is an ordeal dreaded by the patient. In our first attack on this problem we attempted to relieve pain by the application of ointments containing local anesthetics, but the results were so disastrous that we soon discontinued their use. In most cases ulcers enlarge

TABLE VI—HEALING OF ULCERS

	Patient with ulcers	Healed	Unhealed	Dead or amputated
Typical thrombo-angiitis obliterans	224	153	33	38
Borderline cases	31	21	6	4
Totals	255	174	39	42

rapidly under such ointments and healing is markedly delayed. We, therefore, returned to the method of producing anesthesia of the ulcerated area by blocking the peripheral nerves, as suggested by the writer in 1922.<sup>2</sup> Later this method was modified by exposing and sectioning the nerves instead of injecting them with alcohol. This procedure has proved exceedingly valuable and satisfactory. Of the 255 cases with ulcers, 25 had pain considered severe enough to require operative relief. The details of this treatment and the results obtained have been published elsewhere (5) but they may be briefly summarized. The nerves were exposed by small incisions above the ankle, sectioned, and immediately sutured. Primary union of the operative wounds was almost invariably obtained. Relief of pain was complete in practically all cases. Since only the intrinsic muscles of the foot were paralyzed, no interference with walking resulted from the operation. The sensitive wound surfaces became anesthetic, they could be cleaned and dressed without pain, and appeared to heal more rapidly. No trophic ulcers resulted, and return of sensation in the feet took place in approximately a year. By this simple operation, the problem of severe pain can be met and overcome. It is no longer necessary to amputate an extremity for this reason alone.

It is important to emphasize that in many cases the ulcers healed have been of enormous size. Photographs of several such healed ulcers illustrate this point. In all of the cases selected for illustration, the disease was far advanced and impairment of circulation was extreme. Nevertheless, by persistent treatment with injections of hypertonic saline solution and the additional measures described, satisfactory and lasting healing of the wounds has been achieved. Recurrence of ulceration has been infrequent, and occurred chiefly in those patients who resumed smoking.

<sup>1</sup>Desitin ointment (Desitin Manufacturing Co., Providence, R.I.) contains codliver oil and Dakin's solution in a bland base.

<sup>2</sup>The method of producing anesthesia of an ulcerated area to relieve pain by nerve block was published by the writer in 1922 as a supposedly original contribution. Only a few months ago I discovered that Quéna had thought of the same procedure in 1893. He reported its use in three cases in 1910 (6, 9) and apparently never again called attention to it.

## OTHER CRITERIA OF IMPROVEMENT

While preservation of the extremities and the healing of ulcerative and gangrenous lesions are the most convincing evidence of the value of the intravenous saline method of treatment, other evidences of improvement may also be cited. These consist of relief of pain, improvement in walking, increased oscillometer readings, increased temperature of the involved extremities, return of pulsation or development of new pulsations in the feet, improved growth of the nails, and marked improvement in the general health of the individuals. Four hundred and thirty-four or 83 per cent of the 534 patients treated responded to a greater or lesser degree in this manner. A few typical instances are cited as fair examples of what may be expected.

D. W. aged 39 years, window cleaner by trade, was first seen in April, 1925 (which time he complained that for 6 months he experienced increased difficulty in walking. He could walk only one block without stopping on account of pain in the left calf. There was no history of migrating phlebitis or of any other serious illness. Since the age of 26 years, he had smoked about 30 cigarettes daily.

Examination revealed a well nourished young man. The general physical examination was negative. Both femoral and the right popliteal arteries were pulsating. The left popliteal was closed. The right anterior tibial was open. There was no other pulsation in the right foot, and no pulsation in the left foot. There was small ulcer on the left big toe. The oscillometer readings were left calf, left ankle, right calf 5 right ankle, 6. (Average normal oscillometer readings are calf, ankle, 5.)

Shortly after treatment was begun, gangrene of the left first and second toes developed. The patient was admitted to the hospital and conservative treatment was continued until sharp demarcation of the gangrenous area had occurred. He was then returned to the Out Patient Department. Here he was given crutches and advised to rest as much as possible. Saline injections were continued three times a week, and after the gangrenous tissue sloughed away, dressing as applied to the ulcerated surface. By March, 1926, 3 months after treatment was begun, the foot was entirely healed. In April 1926 he could walk 6 blocks without stopping, and the oscillometer readings were left calf, 3 1/2 left ankle, 3 right ankle, 3.

Treatment was reduced to once a week and in July to once a week. At this time he was allowed to return to work. Treatment was discontinued entirely in December, 1926. In March, 1927, he was examined. He reported that he was working regularly, not smoking, and that his foot had resumed healed for 3 years. He had no pain and could walk fifteen blocks without stopping. The oscillometer readings were left calf 3 left ankle, right ankle 7.

Thus in spite of an oscillometer reading of and gangrene of two toes, complete healing was accomplished in 1 year and the substantial improvement of circulation has continued for 3 years. Patient is entirely free of symptoms and fully restored economically.

H. F. aged 30 years, operator, first seen in February, 1927, gave history of intermittent claudication for 6 months and severe pain in the right foot for 3 weeks. There was no ulceration. He had smoked twenty cigarettes daily since the age of 14 years. No history of other serious illness and no history of migrating phlebitis.

General physical examination was negative. The circulation in the left lower extremity was relatively normal. The right femoral and popliteal vessels were open but there was no pulsation at the right ankle. The right foot was erythematous and blue. The oscillometer readings were left calf, 6 left ankle, 3 1/2 right calf, 3 1/2 right ankle, 2.

This patient was advised to rest in bed and was started on saline injections three times a week. After 6 weeks of treatment he was much improved, and the pain was much less severe. In April his foot was noticeably warmer and the nails showed signs of new growth. In July 3 months after treatment was begun, he was allowed to return to work. In April, 1928, he could walk eight blocks without pain, and the return of feeble pulses was noted in the right anterior tibial artery. The oscillometer readings were left calf, 6 left ankle, 5 right calf, 5 right ankle, 4.

At this time treatment was reduced to once a week, and it was discontinued entirely in November 1928. He has been repeatedly examined since then, the last time in May, 1934. He is working regularly, he does not smoke, he can walk now to right blocks rapidly and any distance slowly, and is entirely symptom free. The right anterior tibial pulse is open and the oscillometer readings are left calf, 4 1/2 right calf, 4 right ankle, 2.

This patient was a precarious case when first seen, with a cold blue foot and a zero oscillometer reading at the ankle. He was completely restored in 18 months and has now continued in excellent condition without any recurrence for seven years.

D. P. merchant, aged 33 years, was first seen in April, 1929, 1 1/2 hours before his history of migrating phlebitis of both legs for 1 year. Ulceration had been present on the big toe of the left foot for 3 months, and on the big toe of the right foot for 3 weeks. He had been treated with typhoid vaccine injections and administration of large quantities of fluid by dextrose tube without benefit. He smoked about twenty cigarettes daily.

Examination showed a well nourished young man. Circulation of the upper extremities was normal. Both femoral and both popliteal arteries were open. A good pulsation was felt on the outer side of the left ankle. No other pulsations could be felt in either foot. There were two gangrenous ulcers on the left big toe, each of which measured 1 centimeter in diameter. There was single gangrenous ulcer of the same size on the right big toe. There was smaller ulcer on the right second toe. The oscillometer readings were left calf, 3 1/2 left ankle, 3 1/2 right calf 4 1/2 right ankle, 3 1/2.

He was admitted to the hospital and treated with rest in bed, intravenous injections of hypertonic saline solution three times a week, and surgical care of the ulcers. In 3 months the left foot was entirely healed. His only wound ulcer on right big toe. At this time he was discharged from the hospital and subsequent treatment was continued at the office.

In December, 1930, after 8 months of treatment, the right foot was also healed. At this time the patient could walk three blocks without stopping. A good pulsation was now felt on the outer side of the right foot, and the pulsation on the outer side of the left foot was improved. Oscillometer readings were now left calf 3 left ankle, 3 1/2.

right calf, 5, right ankle,  $\frac{1}{2}$ . The treatments reduced to once a week were continued until September, 1932.

Examination at this time revealed good pulsations in both feet. The oscillometer readings were left ankle,  $2\frac{1}{2}$ , right ankle,  $1\frac{1}{2}$ . Walking had shown further striking improvement. He was last examined in June, 1934. He had remained in good condition without treatment and was active in his business. There had been no recurrence of trouble in his feet. The pulses were present as previously noted, in both feet. The oscillometer readings were left ankle, 3, right ankle, 2.

This patient had fairly advanced thrombo-angitis obliterans, with gangrenous ulcers on both feet when first seen. After 8 months of treatment, both feet were healed and there was improvement in walking. Four years after treatment was first begun, he is in excellent condition, without recurrence of trouble in his feet, and is able to carry on his business without hindrance.

C F, printer, aged 48 years, was first seen July 14, 1932. Eight years previously he began to have intermittent claudication in the left leg. This was followed by gangrene of the left foot and loss of the first, second and third toes of this foot. During the next 7 years, ulceration of the fingers of both hands occurred from time to time, and healed spontaneously. Three months before he was first seen, he began to have intermittent claudication in the right leg after walking one block. Following this, gangrene of the four inner toes of the right foot developed, and at the same time gangrene of the terminal portion of both thumbs and the right index finger set in. He had been a heavy smoker since the age of 12 years.

Examination showed an emaciated middle aged man. All vessels were open in the upper extremities, but the radials were very small. There was gangrene of the terminal phalanges of both thumbs and a gangrenous lesion on the dorsal surface of the right index finger. Both femorals and both popliteals were open. No pulsation could be felt at either ankle. There was an extensive area of gangrene involving the inner four toes of the right foot extending on to the dorsum and plantar surface of the foot. The oscillometer readings of the lower extremities were left calf, 3, left ankle,  $\frac{1}{2}$ , right calf, 2, right ankle, very very faint.

This patient was admitted to the hospital, and because of the severe pain, section of the nerves of the right foot was performed. Complete relief of pain in the foot resulted from this operation but some pain in the gangrenous fingers persisted. He received injections of saline three times a week and surgical care of the wounds. Healing was relatively rapid. Nine weeks after his admission to the hospital he was discharged with a fairly clean granulating wound on right foot measuring about 4 by 2 inches. Subsequently, the saline injections were continued at the office three times a week.

In November, 1932, after 5 months of treatment, all the fingers were healed and the ulcer on the right foot measured 1 by  $\frac{1}{2}$  inch. In February, 1933, after 8 months of treatment, the right foot was entirely healed. Patient was allowed to walk and return to work at this time. His treatment was reduced to once a week, and has been continued until the present time. He was examined in April, 1934, and appeared in excellent condition. He has been working without interruption and has had no recurrence of ulcers on his foot. Sensation in the right foot has returned almost completely. There is still no pulsation in either foot. The oscillometer readings are left ankle,  $\frac{1}{2}$ , right ankle,  $\frac{1}{2}$ .

This patient represented an advanced instance of thrombo-angitis obliterans involving all four extremities, with extensive gangrenous ulcers on three extremities. After 8 months of treatment, all his wounds were healed and he was allowed to return to work. He has remained in excellent condition since then, without recurrence of trouble. It is noteworthy that improvement was accomplished in this case in spite of very serious impairment of circulation.

H H, barber, aged 40 years, was first seen March 14, 1924. For 6 months he had intermittent claudication of the left leg and pain in the left big toe. Three weeks before he was first seen, the toe was cut by a chiropodist and an extensive wound resulted. Since then pain had been very severe and could not be relieved with large doses of sedatives. Patient had been a heavy smoker since boyhood.

Examination revealed a fairly well nourished man who was suffering severely. Circulation of the upper extremities was normal. Both femoral and the right popliteal arteries were open. The left popliteal was closed. No pulsation could be felt in the left foot. This foot was swollen and there was an ulcer on the dorsal surface of the big toe which measured 2 centimeters in diameter. Treatments with injections of hypertonic saline solution were begun in March and were given three times a week. In May, 1924, injection of the posterior tibial nerve with alcohol was carried out for relief of pain. Treatment was continued with the patient ambulant on crutches, and by the end of September, 1924, the ulcer was completely healed. At this time the patient returned to business and has continued at his regular occupation during the 10 years since then without interruption and without any recurrence of trouble in the foot. He has been examined from time to time, and, on his last examination, in February, 1932, both pulses were present in the right foot. There was still no pulsation in the left foot. The oscillometer readings were as follows: left calf, 1, left ankle,  $\frac{1}{2}$ , right ankle, 3.

A letter was received from this patient in February 1934. He stated he could walk from ten to twelve blocks without stopping, was continuing at work as a barber, and had had no recurrence of trouble in his feet.

This case is presented because it illustrates that in spite of marked impairment of circulation, healing was accomplished in a period of 7 months, and that during a follow-up period of 10 years no recurrence of trouble in the feet was noted.

Unfortunately advanced cases of the disease frequently do not begin to show improvement until treatment has been given for 6 weeks or longer. Many such individuals become discouraged and discontinue treatment before an adequate trial can be made. These constitute the majority of the cases listed as unimproved. It is important to inform patients at the start that improvement in their symptoms will not be apparent immediately, and that they must have patience and persistence. In due course of time improvement begins, and then there is no further trouble in persuading them to continue with the treatment.

## DANGERS AND CONTRA-INDICATIONS

It may be confidently stated that the treatment of patients with thrombo-angitis obliterans by means of repeated intravenous injections of hypertonic saline solution is absolutely without danger or harmful effect. Over 5,000 injections of this kind are given every year by me, or under my direct supervision and the total number of treatments which have been given is well over 35,000. There have been no deaths nor accidents of any kind. Infrequently a patient treated in the Out Patient Department of the hospital developed transient jaundice, which disappeared on cessation of injections, without any sequelae. No explanation of this jaundice has been found. It is puzzling since no instance of jaundice ever appeared in the large number of cases treated in an exactly similar manner in my private practice.

Thromboses of the superficial vein at the site of injection will take place if the vein is unduly traumatized or if the patient continues to smoke. With reasonable care and good co-operation by the patient, it is frequently possible to use the same vein for months without any difficulty.

This method of treatment has not been employed if patients presented evidence of serious cardiac or renal disease. It is contra-indicated in patients over 60 years of age. It has no place in the treatment of Raynaud's disease or other allied vasomotor and trophic disturbances.

A discussion of the rationale of this method of treatment is purposely avoided in this paper as it rests on theoretical grounds, and the positive results obtained speak for themselves. It is only necessary to answer the following criticism by Brown and Allen of the Mayo Clinic which appeared in 1925. "It is probable that much of the relief which is obtained from various forms of intravenous solutions owe whatever effectiveness they may produce to certain contaminations and non-specific protein reactions" (1) and which is repeated by Brown in 1924. "Injections of hypertonic salt solution have been used with good results. In my opinion, their efficacy depends on the mild fever induced" (2). "Many of my patients have been treated for weeks and months in the hospital and temperatures have been recorded carefully. Any temperature reaction after injection is exceedingly rare. There are no chills and nothing to indicate a foreign protein reaction. Evidence in support of the statements quoted above is completely lacking in my experience."

A brief statement may be added pointing out the advantages of the method of treatment em-

ployed in this series of patients. It is a simple form of treatment, requiring no expert knowledge or technique, and can be carried out by any physician in his office. It subjects the patient to no dangerous operation, requires no hospitalization, and unless the condition is advanced, does not even require cessation of employment. It is absolutely safe, and for its successful use requires only reasonable care, persistence and patience.

## SUMMARY

During the past 10 years, 324 patients with thrombo-angitis obliterans have been treated by means of repeated intravenous injections of 5 per cent sodium chloride solution.

Improvement has resulted in 434, or 83 per cent, of these cases, evidenced by cessation of pain, improvement in walking, increase of oedihometer readings, increased temperature of extremities, healing of ulcers, and reopening of obliterated vessels.

No dangerous reactions or untoward results have been noted in over 35,000 injections.

Seven and six tenths per cent of all patients treated have required amputation of an extremity.

## CONCLUSIONS

Thrombo-angitis obliterans is not a progressive disease if patients discontinue the use of tobacco.

Repeated intravenous injections of hypertonic salt solution is a simple and effective method of treatment for this condition.

## BIBLIOGRAPHY

1. AMORY, A. W. and BROWN, GEORGE E. Thrombo-angitis obliterans. *J. Am. M. Ass.*, 1924, 90, 180.
2. BROWN, G. E., ALLEN, E. V. and MARSHALL, H. R. Thrombo-angitis obliterans. p. 145. Philadelphia, W. B. Saunders Co., 1924.
3. BROWN, G. F. Thrombo-angitis obliterans. *Surg. Gynec. & Obst.*, 1924, 38, 707.
4. DEER, JULIO. La Tromboangitis Obliterans. Buenos Aires, Casapell & Co., 1924.
5. LARLEY, A. F. and SILBERT, S. Thrombo-angitis obliterans, relief of pain by peripheral nerve section. *Ann. Surg.*, 1923, 86, 33.
6. QUESNE, E. De la douleur dans la gangrene et son traitement par la névrotomie d'urgence. *Bull. Med.*, 1920, 24, 664.
7. SILBERT, S. The treatment of thrombo-angitis obliterans by intravenous injection of hypertonic salt solution. preliminary report. *J. Am. M. Ass.*, 1924, 86, 720.
8. IDEM. Thrombo-angitis obliterans; results of treatment with repeated injections of hypertonic salt solution. *J. Am. M. Ass.*, 1925, 84, 720.
9. VIGOROUS, M. La névrotomie dans la gangrene des membres. Reported for Quebec. *Bull. Acad. de Med.*, 1904, 3, 1.

# JEJUNAL DIVERTICULOSIS<sup>1</sup>

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**M**ULTIPLE jejunal diverticulosis is a rare condition. The diverticula are outpouchings of the gut wall which possess mucous membrane that is continuous with that of the intestine. When situated on the mesenteric aspect of the intestine, as virtually are all the acquired diverticula, they have been characterized erroneously as mesenteric cysts. The term "diverticulosis" is strictly applicable to the condition of multiple uncomplicated diverticula.

Jejunal diverticula may be divided into two distinct anatomical groups: the congenital and the acquired. The acquired often referred to as "false" are those said to be postnatal in origin. Their walls consist of only a fraction of the anatomical layers of jejunum, usually the circular and longitudinal muscle tunics are absent.

Congenital jejunal diverticula result from inco-ordinated embryological development. Their walls are composed of all layers of the normal jejunal wall. Only a few have been reported (J. L. Hunter, Buchwald and Janicke, Miller, and Somerford). They are most often single and usually are situated on the free border. Lewis and Thynng, as well as Poncher and Milles, suggest that these originate from pinched-off nodes of epithelium during the development of the intestine.

The earliest references to false diverticula according to Fischer, are those of Sommering in 1794, and Voigtel in 1804.

Case collected 17 recorded cases up to 1920, Terry and Mugler 19 in 1921, Helvestine 27 in 1923, Sheppe 30 in 1924, Watson 24 in 1924, Rothschild 33 in 1925, whilst Godard in 1927 had evidence of 50 cases. The above collections contain several cases in common. To date the author has been able to find a total of 71 recorded cases.

## INCIDENCE

Jejunal diverticulosis probably occurs more commonly than one would judge from the available reports.

The incidence must be ascertained from radiological and anatomical studies because the clinical picture is not characteristic. However, from radiological study alone the condition may not even be suspected. This is exemplified in Boling's patient, a man 58 years of age, whose pre-operative diagnosis was ruptured duodenal ulcer,

or incomplete intestinal obstruction. On abdominal exploration 250 to 350 jejunal diverticula were seen and an enterostomy was performed. Several months later X-ray studies failed to demonstrate the diverticulosis.

A similar attack occurred 9 months later and this time 153 centimeters of jejunum was resected. This bore 53 diverticula which were considered to be larger than when first examined. In our second case also, X-ray study did not demonstrate the diverticulosis.

Fraser found only one instance of jejunal diverticulosis in 5,000 case records in the Royal Victoria Hospital of Belfast. He gives the following relative frequency of occurrence of diverticula in the gastro-intestinal tract, the first named being the most common: colon, Meckel's, duodenum, pharynx, esophagus, stomach, jejunum. Helvestine also believes that jejunal and ileal diverticula are the rarest of those in the alimentary tract. Gardiner and Sampson studied the figures of three large institutions in this country and those of the City Hospital of Dresden and found 16 cases of acquired diverticula of the small intestine in 14,068 autopsies. Sir Arthur Keith has stated that there are six specimens of jejunal diverticula (one, that from an ox) in the Royal College of Surgeons of England Museum, and in the museums of the various medical schools in London. Larimore and Graham reported finding jejunal diverticula in 3 of 3,446 complete gastro-intestinal X-ray studies. Case, in 6,874 complete X-ray examinations, found 4 cases of jejunal diverticulosis (2 of these were confirmed at operation) and in 1 case diverticulosis of both the jejunum and ileum. In the same series he found diverticula of the duodenum eighty-five times.

In 5,000 autopsies at the Buffalo City Hospital, jejunal diverticulosis has been found only three times, 5,000 complete gastro-intestinal radiological studies did not reveal one case.

## ETIOLOGY

Klebs, in 1869, pointed out a relationship of the diverticula to vessels. Since this time many theories of origin have been advanced. These have been reviewed by Fischer, Beer, Helvestine, and Fraser.

Fraser concluded from his studies that the causative factor is "increased intra-intestinal

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trusion acting along the channel for the artery where the longitudinal muscle is divaricated." He has pointed out that in the jejunum, the longitudinal muscle fibers do not completely invest the bowel as do the circular fibers but tend to lie in strands which are more or less well separated from one another and are completely missing at the mesenteric border. The vessels enter the wall of the jejunum where the longitudinal muscle fibers are defective, and these points of entry may be considered as potential sites of herniations. This disposition of the muscle bands is well known. We fixed a number of jejunal segments and by dissection verified this relationship of the muscle fibers.

Butler concluded from experimental studies similar to those of Fraser that the underlying etiological factor is sclerosis of the terminal branches of the superior mesenteric artery. He thinks that when sclerotic cause "traction pockets" which with increased intra-intestinal pressure give rise to diverticula.

Following a somewhat similar technique as these two authors, we have been able to produce very small pouches on the mesenteric side of the jejunum but the intra-intestinal pressure required was greater than would develop during life. The results of this work will be incorporated in a later communication.

#### PATHOLOGY

As stated, the acquired diverticula almost always are found on the mesenteric side of the small bowel. They apparently begin as herniations of the mucosa, tunica propria, and muscularis int. defects of the circular and longitudinal muscular layers. As they enlarge the villi tend to become shorter. The fundus of the individual diverticulum extends between the leaves of the mesentery and it may push forward and overlie the jejunal wall. Several small diverticula may coalesce and the common fundus exhibit a partial cleft which later is obliterated.

The diverticula may range from several to several hundred. Both ileum and jejunum exhibited diverticulosis in several reported cases. Jejunal diverticulosis with multiple diverticulosis of the colon has been reported by Butler and E. A. Johnson. In this regard also, DeWitt Stetten has described the case of a 38 year old woman with two false diverticula on the mesenteric side of the upper ileum associated with multiple diverticulosis of the colon.

The microscopic picture of the uncomplicated acquired diverticulum varies somewhat. Butler stated that in the small beginning diverticula,

both the longitudinal and circular muscle fibers are present but thin. In the well advanced cases, the wall consists only of mucosa, muscularis mucosae and serosa. There may be diminution in size of the epithelium and the villi. The bowel wall contiguous to the diverticula usually shows no departure from the normal. Heijestine has reported diminution in the amount of the circular muscle.

Since the acquired diverticula are devoid of the muscular tunica proper, intrinsic peristalsis cannot occur. Because of this and their bottle neck type of mouth, they tend to act as stagnant pools in the course of the jejunal stream. Radiological findings in some reported cases bear this out. Their emptying necessarily must depend on transmitted peristalsis from contiguous coils of intestine.

Complications of jejunal diverticulosis do not occur frequently.

Inflammation in one or more diverticula has been reported by Bralshaw, Case, Fischer and Butler. Gardiner and Sampson thought that in a case they reported inflammation of a diverticulum gave rise to chronic mesenteritis, which in turn caused "an angular bending of the intestine and partial obstruction of its lumen."

An enterolith in a diverticulum was held responsible for intestinal obstruction by Terry and Mupler and also C. M. Watson. Perforation of a diverticulum was reported by Butler in 3 cases of jejunal diverticulosis.

#### CASE REPORTS

CASE. T. P. A white male, aged 60 years, entered the Buffalo City Hospital, June 9, 1935. His complaints of frequency, urgency, nocturnal incontinence of 3 months' duration, pain in the back, and partial phosia. He had lost 30 pounds in weight.

There are no symptoms referable to the gastrointestinal tract other than anorexia. Emaciation is marked. Some of the teeth were carious. The patient was anorectic but reacted to light and accommodation. The heart was enlarged slightly to the left and there was double aortic murmur. The patellar reflexes were sluggish. Cystoscopic examination revealed an irritable, firm, friable reddened mass in the bladder. A biopsy of this was reported as carcinoma. Urinalysis specific gravity 1.020. A. albumen ++, blood ++, blood W. 100,000, 4 phos. Hemoglobin 60 per cent (Tallquist). Erythrocytes 1,500.

Hematuria continued and the clausal course was progressively downward. There was some blood in the sputum. Laryngoscopic examination was not possible because of the patient's weakness. Death occurred June 21, 1935. A biopsy was performed 6 hours after death.

The anatomical diagnoses were: acute mesenteritis with abscesses of thoracic aorta; carcinoma of the urinary bladder; pulmonary emphysema; chronic (lower) pleurisy; chronic interstitial nephritis; cardiac hypertrophy; multiple diverticulosis of the jejunum; Tinea vaginata; infection.



Fig 1 Photograph of portion of jejunum of Case 1 Multiple diverticula Arrow indicates head of *Tænia saginata*.

There were 24 thin walled diverticula in the first 3 feet of the jejunum—some were pea sized, others were as large as a horse chestnut. They all were on the concave aspect of the bowel and projected between the leaves of the mesentery. Branches of the mesenteric vessels were in relation to their fundi. The ostia of the diverticula varied in diameter from 1.4 centimeters to 0.2 centimeter and opened into the intestinal lumen. The villi, when present in some of the diverticula, were atrophic. The mesentery did not contain an unusual amount of fat. The mesenteric lymph nodes were slightly enlarged and partly fibrosed. The mesenteric arteries were not sclerotic.

A *Tænia saginata*, 55 inches long, lay coiled in the proximal portion of the jejunum. Its head was attached to the ostium of one of the diverticula.

Microscopically both the longitudinal and circular muscle layers tapered rather sharply near the ostia of the diverticula and were entirely deficient in their wall and fundus. The mucosa rested directly on the serosa which exhibited some fibrous thickening. There were no inflammatory changes.

**CASE 2** M. G. A white male, aged 73 years, was admitted to the Columbus Hospital, May 10, 1933, complaining of epigastric pain, nausea and vomiting after meals, and dysphagia. There were no other gastro-intestinal symptoms. Physical examination was essentially negative. The blood Wassermann was 4 plus. X-ray studies showed some irregular narrowing of the esophagus and a persistent deformity of the pyloric end of the stomach. The latter was empty in 4 hours. The 6 and 24 hour films did not show any evidence of intestinal diverticula. Death occurred June 17, 1933.

An autopsy was performed 48 hours after death.

The anatomical diagnoses were carcinoma of the esophagus with extension to the stomach and metastases to the liver and regional lymph nodes; luetic mesenteritis; emaciation and anemia; parenchymatous degeneration of



Fig 2 Photograph of portion of jejunum, Case 2 Note four of the larger diverticula

the heart, kidneys, liver, and spleen, cardiac dilatation, jejunal diverticulosis.

On the concave aspect of the proximal 16 inches of the jejunum, there were 15 diverticula varying in size from a small bean to that of a walnut. These were thin walled, and their fundi were in relation to vessels. The diameter of the ostia was generally about one fourth of that of the diverticula. The mesentery possessed the usual amount of fat. The lymph nodes were not remarkable. The mesenteric arteries were not sclerotic.

Microscopically the muscular tunics of the jejunal wall tapered in their approach to the diverticula, and in the diverticula walls were missing, and the mucosa was in direct contact with the serosa. There were no inflammatory changes.

**CASE 3** A white female, aged 62 years, entered the Buffalo City Hospital, January 26, 1934, complaining of inability to move the left arm and left leg. On this occasion, as in a previous clinic admission, there was no mention of gastro-intestinal symptoms.

There was flaccid paralysis, a bilateral Babinski response, and hyperactive knee jerks. The heart was enlarged to the

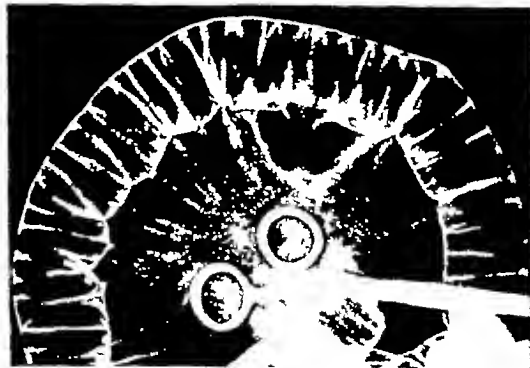


Fig 3 Photograph of contrast X-ray study of portion of jejunum of Case 3 Note the valves and relatively small ostium of the large diverticulum



Fig 4. Portion of colon of Case 3. Photograph of contrast X-ray study. A great number of diverticulae are seen.

left and there was blowing systolic murmur over the apex. The blood pressure was 78/33. Abdominal examination was negative. On admission the temperature was 99 degrees F and the pulse 100 per minute; these rose terminally to 104 degrees and 118 per minute, respectively.

The blood Wassermann was negative. The blood urea was 45 g milligrams per 100 cubic centimeters. Urinalysis was not remarkable. There were no X-ray studies. Death occurred January 3, 1934.

The autopsy was performed 7 hours after death.

The anatomical diagnoses were: general arteriosclerosis, coronary atherosclerosis, cerebral arteriosclerosis with cerebral atrophy, multiple diverticulosis of the jejunum and colon,



Fig 6. Photomicrograph of one of the smaller diverticula of Case 3. Note the relation of the vessels to the fundus. X4.



Fig 5. Photograph of portion of jejunum of Case 3. The mesenteric fat has been dissected away and the mesenteric vessels injected with red gelatine to show their relation to the diverticula.

mesenteric defect with herniation of the small intestine, chronic bronchitis, pulmonary emphysema, chronic hypertrophic arthritis.

There were 5 diverticula on the mesenteric aspect of the first 20 inches of the jejunum. Three varied in greatest diameter from .5 millimeters to 4.5 centimeters. They were thin walled and were in relation to vessels. The ostia of the 2 smaller ones were approximately equal to their fundus diameter, while the mouth of the largest one was one-third the fundus diameter and was guarded by two valve like folds. The villi within this one were quite trophic. In the odd portion of the mesentery there was defect measuring 8 by 1 centimeters. The borders of this were fibrously thickened and loop of small bowel



Fig 7. Photomicrograph of small diverticulum of Case 3. In the fundus the smooth muscle is entirely defective. X4.

protruded through this defect. The mesentery possessed a slightly increased amount of fat. The mesenteric arteries were not sclerotic. The lymph nodes were not remarkable. In the colon also there were about 250 thin walled diverticula which varied in size from 0.5 to 2.0 centimeters in their greatest diameters.

The microscopic picture of the jejunal diverticula was similar to those of the 2 other cases.

In 5,000 autopsies, multiple diverticulosis was found only three times. Of these 3 patients, all of whom were in the fifth decade, 2 had organic syphilis. The microscopic features were similar in all 3 cases.

In relation to the stated theories of etiology of jejunal diverticulosis, it is interesting to note that the mesenteric arteries in all 3 cases were not sclerotic. Nor was there an unusual amount of mesenteric fat. In the third case, where there was a mesenteric defect with herniation of the lower portion of the jejunum and ileum, it is possible that a chronic intermittent intestinal obstruction, even of a low degree, could have increased the intra-intestinal tension and thereby have been an etiological factor, as suggested by Butler.

The relation of the coils of the *Tænia saginata* to the diverticulosis is purely speculative. For it to have been a causative factor, we must assume that the *tænia* was there a long time, and that it was responsible for an increase in the intra-intestinal tension. Although this seems to us to be highly improbable, cases have been reported in which the *tænia* was considered a factor in perforation with peritonitis, from suddenly increased intra-intestinal pressure.

The first recorded case of parasitic infestation of the jejunum with multiple diverticulosis is that of Goinard and Courrier. Their patient died following an operation to relieve what clinically appeared to be a bowel obstruction. In the lumen of the jejunum and in the intra-epithelial cysts within diverticula, there were "segmented eggs, larva and blastomeres," of the *Strongyloides intestinalis*. These authors thought that the parasites were in some way a cause of the diverticulosis, but freely admitted a lack of proof for this assumption.

Constipation has been charged with contributing to the development of diverticulosis through increasing the intra-intestinal pressure. In diverticulosis of the colon, chronic constipation would seem to be more definitely established as a causative factor than in jejunal diverticulosis. A history of constipation was conspicuously absent in each of our cases.

Most patients with jejunal diverticulosis are free from gastro-intestinal symptoms. In some

recorded cases there has been pain 1 to 3 hours after eating, nausea, vomiting, distention, and borborygmus relieved by change in body position. Other reported symptoms are melena, constipation, and in 2 cases (Braithwaite and MacKechmie) a fecal taste associated with vomiting. Some have presented a syndrome interpreted as a low grade intestinal obstruction which required surgical intervention. In general the symptomatology, when present, may be said to resemble that of the so called chronic duodenal ileus. The most positive diagnostic criterion is the finding of multiple pouches with fluid levels in the midabdomen, with the use of the roentgen ray and radioopaque meal. Our cases like the majority of those reported were symptomless.

#### SUMMARY

1 The literature concerning jejunal diverticulosis has been reviewed and the incidence, pathology, and symptomatology discussed.

2 Three cases of jejunal diverticulosis have been presented.

3 One of these, so far as we know, is the fourth recorded case of multiple diverticulosis of both the jejunum and colon in the same individual. One is the second recorded case of jejunal diverticulosis with an associated parasitic infestation of the jejunum.

#### BIBLIOGRAPHY

- 1 BEER, E. Some pathological and clinical aspects of acquired (false) diverticula of the intestine. *Am. J. M. Sc.*, 1904, 128, 135.
- 2 BOLING, J. R. Multiple diverticula of small intestine. *J. Am. M. Ass.*, 1930, 95, 267.
- 3 Idem. Multiple diverticula of jejunum with resection. *J. Am. M. Ass.*, 1931, 96, 526.
- 4 BRAITHWAITE, L. R. A case of jejunal diverticula. *Brit. J. Surg.*, 1923-1924, 11, 184.
- 5 BUCHWALD, A., and JANICKE, O. Ueber Darmcysten (Enterokysten) als Ursache eines kompletten Darmverschlusses. *Deutsche med. Wchnschr.*, 1887, 23, 868.
- 6 BUTLER, R. W. Observations upon multiple intra-mesenteric diverticula of the small intestine. *Brit. J. Surg.*, 1933, 21, 329.
- 7 CASE, J. T. Diverticula of small intestine other than Meckel's diverticulum. *J. Am. M. Ass.*, 1920, 75, 1463.
- 8 FISCHER, M. H. False diverticula of the intestine. *J. Exper. Med.*, 1900-1901, 5, 333.
- 9 FRASER, I. Diverticula of the jejuno-ileum. *Brit. J. Surg.*, 1933, 21, 183.
- 10 GARDINER, H. C., and SAMPSON, J. A. Diverticulitis (not Meckel's) causing intestinal obstruction. *J. Am. M. Ass.*, 1906, 46, 1585.
- 11 GODARD, H. *Rev. de chir.*, 1927, 65, 22. Quoted by Fraser.
- 12 GOINARD, P., and COURRIER, R. Sur La Constatacion de Parasites Dans Des Diverticules Multiples du Jejunum. *Ann. d'Anat.*, 1929, 6, 188.

3. HELLMUTH, F. False diverticula of the jejunum. *Berg. Gynaec. & Obst.*, 922, 37.
14. HERTZ, J. L. A mesenteric cyst of jejunal origin complicated by retroperitoneal position of the transverse colon. *Brit. M. J.* 922, 800.
5. JOHNSON, E. A. Diverticula aperta intestinalia. *Amerikan. Med. Gaz.*, 905, 5, 533.
6. KATZ, A. Diverticula of the alimentary tract of congenital or of obscure origin. *Brit. M. J.* 910, 376.
7. LEWIS, F. J. and THURLO, F. W. The regular occurrence of intestinal diverticula in embryos of pig, rabbit, man. *Am. J. Anat.*, 907-1908, p. 505.
8. MACKENZIE, H. N. Diverticula of the jejunum. *Ann. Surg.* 9, 74, 96.
9. MILLER, A. M. Isolated diverticulum of the jejunum. *Am. J. Surg.*, 93, 6.
20. POWERS, H. G. and MILLER, G. Cysts and diverticula of intestinal origin. *Am. J. Dis. Child.*, 933, 45, 664.
1. ROTHSCHILD, N. S. Diverticula of the jejunum. *Ann. Surg.*, 925, 82, 290.
- SEMPER, W. H. False diverticula of the jejunum. *J. Am. M. Ass.* 924, 8, 1.
3. SCHERER, A. E. Two cases of intestinal cancer in infancy: congenital diverticulum of the jejunum. *Lancet*, 920, 215.
23. SHERRIN DAWITT. Multiple diverticula of the upper ileum. *Am. J. Surg.* 91, 75, 245.
5. TIER, W. I., and MILLER, F. R. Diverticula of the jejunum. *Arch. Surg.* 92, 147.
25. WILSON, C. S. Diverticula of jejunum. A case with enterolith causing intestinal obstruction. *Surg. Gynec. & Obst.* 924, 25, 67.

PRIMARY NEOPLASMS OF THE FEMALE URETHRA<sup>1</sup>

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JUDGING from the reports in the literature, the female urethra enjoys a relative immunity to malignant disease. However, it has been suggested that clinicians have either failed to recognize the lesions or failed to report them.

In general, primary neoplasms of the female urethra are divided into two groups: carcinoma and sarcoma.

## CARCINOMA

The first carcinoma of the urethra was reported, in 1833, by Boivin. The early reports were in some cases so incomplete and their evidence so unconvincing that a correct estimation of the lesions is impossible. Among some of the interesting articles published are those of Whitehouse, Percy, Shaw, Palmer, Scholl and Braasch, Mikulicz-Radecki, and Counsellor and Paterson.

## ETIOLOGY

The etiology of carcinoma of the urethra is unknown. From the anatomical structure it is possible for carcinoma to arise from the mucous membrane, para-urethral glands, and their corresponding ducts. Since the majority of early lesions are located near the meatus, and since the large percentage of lesions are of the squamous cell type, it is possible that the para-urethral duct emptying on either side of the external urethral orifice which is susceptible to infection and trauma is a frequent seat of the primary growth.

*Predisposing factors.* Ehrendorfer, in 1899, called attention to local inflammatory processes, trauma, fissure and scars produced by labor as predisposing factors. Venot and Parcelier reviewed 87 cases and noted that in 45 of 47 cases the patients were married. Of the patients with children, the average number was 5. Nine of the 10 patients in the present series were married. Four of the patients had one or more children.

Urethral caruncle as a causative factor is still questionable. The term "caruncle" as used by many physicians, is ill defined, and in spite of the cases reported as arising from caruncles, it is questionable whether the original lesions were true caruncles. Although it is possible for benign growths of the urethra to undergo malignant change this condition is thought improbable. Chronic irritation produced from infection and trauma, as in malignant lesions elsewhere in the body, should be considered as important factors predisposing to malignant change.

## INCIDENCE

Counsellor and Paterson, in February, 1933, with their 12 cases increased the total number of authentic cases to 136. Pomeroy, in 1934, reported 3 cases. The present series of 10 cases brings the total to 149. English, in 1907, found 3 cases in 4,000 autopsies. In approximately 43,000 admissions to the Sloane Hospital for Women from 1919 to 1934, only 1 case of carcinoma of the female urethra was found.

## AGE

Venot and Parcelier, in their review of 87 cases, report an average of 53.4 years. Mikulicz-Radecki, in 14 cases, report 6 over 60 years, 6 between 40 and 60 years, and 2 under 40 years. Counsellor and Paterson, in 12 cases, report an average of 52 years. In the present series of 10 cases, the average is 55.5 years. Therefore, the average age in 109 cases is 53.4 years.

## LOCATION

In many of the reported cases and in 4 cases of the present series, it is impossible to identify the original site of the malignant growth because when first seen the lesion was so advanced that it involved both the anterior and posterior urethra. In 5 of the 10 cases studied, the lesion was located in the anterior urethra. A survey of the cases in the literature leads one to believe that the large majority of lesions are located either in the anterior urethra or in the entire urethra.

## SYMPTOMS AND SIGNS

No essential difference has been noted between the symptoms and signs of carcinomata and adenocarcinomata of the female urethra, and for this reason they are studied clinically as a group.

Carcinomata of the urethra grow slowly and present no characteristic early symptoms or signs. The majority are first seen by a physician in the late stages of the disease, yet the complaints are of relatively short duration. The extent of the lesion as compared with the recent development of signs and symptoms has, in the past, been the most important diagnostic aid. Growths at or near the meatus produce visible tumefactions which are often the first indication of the disease. Of the 5 cases presenting lesions in the anterior urethra, in the present series, 3 complained of

<sup>1</sup>Work done in the Squier Urological Clinic, Presbyterian Hospital, New York.



Fig. P. N. 89. The photomicrograph presents clumps of small rounded or oval cells which have tendency to form glands and secrete mucus. There is but slight variation to be noted in the size and in the shape of these cells.  $\times 85$



Fig. P. N. 879. The photomicrograph presents a free arrangement of round-oval cells. The cells are well-circumscribed in a disordered arrangement. In other sections of the tumor the cells have tendency to form glands and secrete mucus.  $\times 85$

tumefaction in the urethra as one of the first symptoms and signs.

A survey of the symptoms and signs obtained from the present series of 10 cases is as follows:

	Cases	Per cent
Difficulty or retention of urine	6	60
Hematuria	4	40
Tumor or metastasis	4	40
Pain or dysuria	4	40
Frequency	3	30
Watery discharges from the meatus	3	30

It is interesting to note that of the 6 cases in which there was difficulty in voiding or of retention of urine, 5 presented either papillary growths or annular growths involving the entire urethra. The sixth case presented irregular elevations in the urethra with marked perirethral induration.

Of the 4 cases complaining of pain or dysuria, only 1 presented ulcerated lesions. Incidentally only 1 of the 4 cases with tender growths presented surface ulceration.

In general, the symptoms and signs of carcinoma of the female urethra are those of obstruction, visible tumor mass, or chronic irritation produced either by infection or trauma.

It must be remembered, however, that a visible metastasis may be the first complaint of the patient. Since lymphatic involvement is of such importance it may be mentioned that the lymphatics

of the female urethra drain into the external iliac, hypogastric, and aortic nodes (Rouviere).

#### CASE STUDIES

Of the 10 following cases, 2 (P. N. 30863 and 30375) have previously been mentioned by Stout (31) in his textbook *Human Cancer*. The author has permitted the use of the cases in the present study. Dr. F. Carter Wood has kindly given permission to use the cases obtained from St. Luke's Hospital. The remainder of the cases have been studied with the permission of the various surgeons whose names are recorded with each case.

Path N. 89 (Dr. J. Rathbone). A colored female, 63 years of age, was admitted to the Squier Urologic Clinic March 8, 1935, complaining for 3 months of difficulty and delay in starting the urinary act. The patient was able to void more freely if she was relaxed. The patient was not married.

An old looking woman presented on examination dark red, pedunculated, soft, smooth mass, protruding from the urethral orifice. The mass was attached 1 pole to the anterior wall of the urethra. Adjoining the first growth was a smaller but similar mass attached by pedicle to the wall of the urethra. At operation March 8, 1935, excision of the tumor masses with fulguration of their bases was performed. The wound healed with no complications. The patient was discharged on March 5, 1935. In October, 1935, 7 months after operation the patient was well and had no complaints. She later left the United States and left no forwarding address.

Microscopic description. There is a solid pleomorphic strand like arrangement of cells. The cells are small,



Fig 3 P N 2227 The photomicrograph presents polyhedral shaped cells with a moderate variation in their size and shape. There is a tendency to form monster cells and to secrete mucin. Some of the cells are vacuolated. The cells are infiltrating in a disorderly manner  $\times 100$



Fig 4 P N 354 The photomicrograph is of a section which presents an irregular infiltration of large round-oval cells which have a tendency to group themselves together and form vacuoles. There is also a tendency to form monster cells  $\times 85$

round-oval with a slight variation in their size and shape. In places the cytoplasm is clear. There is less than one mitotic figure per high power field. The cells have a tendency to form glands and to secrete mucin (Fig 1). There is no keratin, pearl formation, stratification, or intercellular bridges.

Diagnosis carcinoma with a tendency to form glands or adenocarcinoma

Path No 5879 (Dr C Gibson) A female, 58 years of age, was admitted to St. Luke's Hospital on March 16, 1910, complaining of a tender growth in the urethra which had been present for 3 months. The patient noted an associated dysuria and frequency. Although the tumor appeared to decrease in size, the patient had difficulty in voiding. She was married and had no children. On examination the patient did not appear ill but presented a hard, congested tender mass, one half of an inch in diameter, encircling the meatus. The mass was tender and possessed an ulcerating surface. At operation a somewhat encapsulated hard fibrous mass, the size of a walnut, was excised. The patient was discharged in good condition on March 22, 1910. She died in July, 1911, 16 months after operation.

Microscopic description The tissue presents a diffuse arrangement of cells which are round-oval in shape, moderate in size, and with a marked variation in the size and shape. There are on the average three mitotic figures per high power field. The cells have a tendency to form glands and mucin. However, in areas, the cells are infiltrating diffusely in a disorderly arrangement (Fig 2). There is no keratin, pearl formation, or stratification.

Diagnosis carcinoma with a tendency to form glands or adenocarcinoma.

Unit No 38089 (Dr W T Stenson) A white female, 63 years of age, was admitted to the Lenox Hill Hospital on July 1, 1933, complaining of vaginal bleeding and pain on urination of 1 week's duration. Two years previously, because of suprapubic pain and vaginal bleeding, the patient

received a dilatation of the cervix, a curettage of the uterus, and an implantation of radium. The symptoms disappeared for 1½ years but returned 6 months and 1 week previous to admission. Pain on urination, dysuria, and



Fig 5 P N 30375 The photomicrograph presents solid cords of cells lining an irregular central cavity. The cells are oval round with a moderate variation in the size and shape. The cells simulate those of the bladder epithelium.  $\times 85$





Fig. 6 P. N. 379 The photomicrograph presents dense arrangement of spindle cells with moderate variation in size and shape. Mitotic figures may be seen. The tumor simulates closely certain bladder neoplasms.  $\times 85$ .

menstruation developed week previous to admission. The patient was married and had one child. The remainder of her history was negative.

Physical examination revealed a obese white female, not acutely ill, but possessing an enlarged heart and an apical systolic murmur. The length of the urethra extending to

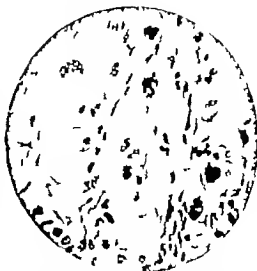


Fig. 7 P. N. 760 The photomicrograph presents bizarre arrangement of cells with an extreme variation in their size and shape. Malignant cells and mitotic figures are noted.  $\times 85$ .

the bladder neck was edematous. Palpation of the anterior vaginal wall revealed it to be indurated. On cystoscopic examination the urethra appeared thrown up in folds and greatly inflamed. Further examination revealed a mass the size of marbles obvi. A biopsy was performed and diagnosis of carcinoma of the urethra made. On July 17

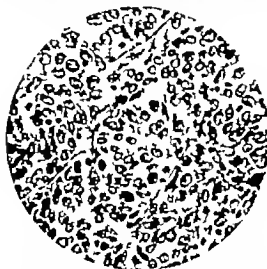


Fig. 8 P. N. 5043 The photomicrograph presents section of lymph node filled with metastatic cells from carcinoma of the female urethra. The cells are round-oval with moderate variation in their size and shape.  $\times 85$ .



Fig. 9 U. N. 5093 The photomicrograph presents intersecting bands of spindle-shaped cells with moderate variation in their size and shape. Some of the cells show vacuoles. One mitotic figure may be seen.  $\times 5$ .

# MENVILLE PRIMARY NEOPLASMS OF THE FEMALE URETHRA

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1933, a transplantation of both ureters in the sigmoid colon was performed. The patient died on July 21, 1933, 4 days after operation, from lobar pneumonia. At autopsy the urethra and bladder neck were covered with a yellow granular tumor mass. The ureteral transplantations were intact.

**Microscopic description** The cells have a tendency to form glands and secrete mucin. There is some variation in the size and shape of the cells but, in general, they are cuboidal in shape and of moderate size. There is less than one mitotic figure per high power field. The cells are infiltrating into the surrounding fibrous and muscle tissue.

**Diagnosis** carcinoma with a tendency to form glands or adenocarcinoma

**Path. No. 2227 (Dr. J. Rathbone)** A white female, 57 years of age, was admitted to the Squier Urologic Clinic on February 21, 1934, complaining of frequency, nocturia, and dysuria for 6 months. Caustic silver nitrate had been applied to the urethra from one to three times a week. Four days previous to admission the patient noted a bright red hematuria. The patient had difficulty in voiding but she was not conscious of it until her urethra was dilated. A gain in weight had been noted. The patient was married and had two children.

The patient appeared healthy but presented on vaginal examination a slightly irregular, non-tender, indurated fixed ridge beginning just posterior to the meatus and extending along the line of the urethra to the bladder neck. On cystoscopic examination, an annular, firm lesion with a white surface involving the urethra and extending to the bladder neck, was found. A minute section of tissue was removed for a biopsy. None of the inguinal glands were palpable.

On March 8, 1934, through a suprapubic opening in the bladder, seven radium needles were implanted around the bladder neck parallel to the urethra. Each needle contained 2.48 milligrams of radium. The radium was removed on March 12, 1934, after a total of 94 3/4 hours. The total amount of radium used was 1,644.86 milligram hours. An abscess of the suprapubic wound developed but this healed with good results. The patient was discharged with a healed wound and with disappearance of all penurethral induration except a mild induration around the anterior urethra.

She is at present, 3 months after the implantation of radium, free of all symptoms. The patient is receiving X-ray irradiation to the inguinal nodes.

**Microscopic description** The cells are polyhedral in shape, moderate in size, and with a moderate variation in the size and shape (Fig. 3). The growth is diffuse with no particular arrangement. There is less than one mitotic figure per high power field. There is a tendency to form monster cells. Some of the cells secrete mucin but there is no glandular formation.

**Diagnosis** carcinoma

**Path. No. 354 (Dr. J. B. Squier)** A white female, 48 years of age, was admitted to the Squier Urologic Clinic on March 26, 1929, complaining of hematuria for 3 weeks and an inability to void for 24 hours. For a year previously the patient had noted lumps in her groins. Several months previous to admission, large amounts of blood were passed in the urine. The patient gave a history of falling 10 pounds in her vagina 2 years previously and losing 10 pounds in weight 1 year previous to admission to the hospital. A hysterectomy was performed at 17 years of age. The patient was married but had no children.

Examination revealed the patient to be poorly nourished and developed. She presented enlarged nodes in each inguinal region and a fixed papillary ulcerated lesion involving the entire urethra. The tumor bled easily. Cystoscopic examination verified the above finding.

On April 10, 1929, 200 milligrams of radium was inserted about the urethral tumor mass. Lead and platinum filters were used. The radium was kept in situ for 6 hours. The total dosage was therefore 1,200 milligram hours. Following this the tumor became less indurated but the ulceration remained unchanged. The vagina became contracted for a May 3, 1929, a margin of the meatus was removed for a biopsy. From April 29, 1929, to June 5, 1929, the patient received twenty two doses of X-ray irradiation over her right and left gluteal regions and over her pubic region. The milliamperes minutes varied from 36 to 61. On June 17, 1929, a partial excision of the left inguinal nodes was performed. On November 4, 1929, 7 months after radium implantation, the patient died. She had previously suffered from agonizing pains. No description of the biopsy was made. The left inguinal node was hard and dense. On cross section, the node appeared pale and dense.

**Microscopic description** There is an invasion of the lining cells together with a diffuse cellular infiltration without any definite arrangement in the cell growth. The cells are round-oval, usually large, but with a marked variation in the size and shape (Fig. 4). The nuclei are large and vesicular and apparently originate from the urethral glands and lining epithelium. There is a formation of monster cells. There is a tendency of the cells to collect in groups and to form vacuoles but there is no true glandular formation. There is less than one mitotic figure per high power field. The section of the left inguinal gland presents cells similar to those of the original tumor. The node is completely filled by the metastatic cells.

**Diagnosis** carcinoma, metastasis to left inguinal nodes

**Path. No. 30375 (Dr. R. Kingsley)** A white female, 52 years of age, was admitted to the Presbyterian Hospital February 21, 1924, complaining of a slow urinary stream associated with a slight pain for 3 weeks and an acute urinary retention of 24 hours following a cystoscopy. Five months previously, the patient had a dysuria for 2 weeks. The patient was married and had two children. She was obese and presented a somewhat tender mass measuring 2 by 6 centimeters which was fixed, bled easily, and extended along the left vaginal sulcus. A tight urethra resisted the passage of a cystoscope. The patient was discharged on March 19, 1924, with the diagnosis of a penurethral inflammation. On March 28, 1924, the patient was admitted complaining of difficulty and pain on voiding. An examination revealed an increased urethral induration associated with tenderness. A cystoscopic examination revealed irregular elevations in the urethra together with much edema of the urethral mucosa. An acute retention of urine followed the cystoscopy.

On April 12, 1924, the urethra with its growth was excised to the vesical orifice and the orifice sutured to the vaginal opening. The patient developed an incontinence of urine. From June 24, 1924, to April 29, 1925, the patient was given nineteen treatments of deep X-ray therapy. The rays were directed anterior, posterior, and lateral to the region of the urethra and on all but two occasions, 180 milliamperes minutes were given. On the two occasions, 40 and 160 milliamperes minutes were given.

Small hard nodules appeared in the left and right arm on August 12, 1924, acute retention of urine developed on December 6, 1924. The urinary stream diminished in size on January 28, 1925. Pain in the urethra associated with bleeding on April 15, 1925. An irregular hard mass in the urethra which prevented the passage of a cystoscope was noted on April 22, 1924. The tissue gave the impression of gristle. The patient died suffering from much pain on November 2, 1925, 19 months after operation.

There are several amorphous pieces of tissue which are firm, trabeculated, dense, and white.

**Microscopic description** The cells are arranged in canoe-like structures, the cells are present in solid groups with irregular central cavities (Fig. 5). The cells infiltrate diffusely in small strands. The cells are round-oval, and moderate in size with moderate variation in the size and shape. There is an average of one mitotic figure per high power field. In general, the cells resemble those of the bladder epithelium. There is no keratin, pearl formation, or stratification.

#### Diagnosis carcinoma

**Path No. 17 (Dr. R. Bolting)** A female, 67 years of age, was admitted to St. Luke's Hospital on December 7, 1933, complaining of discharge from the vulva. Eight months previously the patient noted watery and then bloody discharge from the vulva. The discharge became worse. Previous to admission the patient passed clots of blood from the urethra and noted tender lump in the lower left quadrant. The patient had been gabbling in weight.

The patient did not appear acutely ill. On examination she presented discrete, hard, tender masses in the left groin and hard, sclerotic, tender mass, 3 centimeters in diameter at the urethral orifice which bled easily. The abdomen and radiation was as principally in the anterior urethra.

A biopsy was performed and two small, irregular firm, opaque pieces of tissue were removed.

The patient was discharged to Bellevue Hospital for treatment on January 9, 1934, and the patient was discharged from Bellevue Hospital in February 1934. All attempts to locate her have failed.

**Macroscopic description** The tissue presents cells arranged in the manner characteristic of certain bladder neoplasms (Fig. 6). The cells are oval spindle in shape, with moderate variation in their size and shape. The growth is infiltrating. There is an average of one mitotic per high power field. There is no keratin or pearl formation.

#### Diagnosis carcinoma

**Path No. 0765 (Dr. A. S. Hawkes)** A white female, 43 years of age, was admitted to the Presbyterian Hospital complaining of frequency pain on urination, and hematuria. An increasing frequency for 3 years, an increasing tenderness with sticking suprapubic pain, an occasional right lumbar pain radiating to the groin, and an increasing nocturia for 3 years were noted by the patient. Five weeks previous to admission hematuria which continued for 3 weeks was also noted.

The patient was married and had three children. She was not acutely ill but she presented along the anterior vaginal wall a firm and indurated, somewhat circumscribed mass about the size of walnut located entirely within the urethra on its lower and posterior. All cystoscopic examination revealed much edema about the bladder neck. A wedge shaped piece of tissue was removed from the urethra on July 5, 1934. The indurated mass extended into the bladder. The wound began to slough, the catheter drainage was futile, and the patient suffered lower abdominal pain. She was discharged to Bellevue Hospital on August 27, 1934. She was last seen at Bellevue Hospital on August 27, 1934. All attempts to locate her have failed.

The specimen presented small bits masses of tumor, very resistant to palpation. The tumor appeared to surround the urethra. On cut surface the tumor was white and granular.

**Macroscopic description** The cells present bizarre arrangement and vary greatly in size and shape. In places the nuclei show chromatin divided into multiple parts. Malignant cells are numerous (Fig. 7). There is one mitotic figure per high power field. There is no keratin, pearl formation, or stratification.

#### Diagnosis carcinoma

**Unit No. 5490 (Dr. W. MacFay)** A female, 46 years of age, was admitted to St. Luke's Hospital on January 27, 1934, complaining of tumor at the urinary meatus and bleeding from the urethra. Three months previously the patient noted small tumor at the urethral meatus which became progressively larger, which bled freely and which produced slight amount of pain.

The patient had an acute retention of urine on two occasions years previously and on one occasion 6 years previously. Catheterizations on these occasions were painful. I. & T., bilateral salpingectomy and appendectomy had been performed.

On physical examination the patient did not appear ill, but she presented rounded, firm, slightly pedunculated tumor the size of marble, on the posterior lip of the urethra. The base of the mass was firm and indurated. The tumor bled easily. No lymph nodes were palpable in the inguinal region.

On January 27, 1934, an excision of the urethral mass was performed through vaginal incision. The wound was repaired by suturing the vaginal mucous membrane to the urethral opening. The wound healed and the patient was discharged on February 6, 1934, with no complaints.

On April 22, 1934, the patient presented large fungating mass in the right distal region. She was last seen 37 months after operation. She is now believed to be dead.

Examination of the specimen revealed rounded, firm, papillomatous mass possessing thin fibrous capsule measuring 3 centimeters in diameter with central fibrous pedicle. On section, the mass was smooth, hemorrhagic, and of dense cellular opaque structure.

**Microscopic description** The tissue presents extensive small strands of cells infiltrating into the surrounding tissue. The cells are round and somewhat oval. There is moderate variation in the size and shape of the cells. Many mitotic figures are seen. There is no keratin, pearl formation, or stratification.

#### Diagnosis carcinoma

**Path No. 20663 (Dr. J. C. Connelley)** A female, 45 years of age, was admitted to the Presbyterian Hospital on February 20, 1935, complaining of vaginal discharge. Four months previously she noted which watery discharge from the region of the vagina. Two months previously the patient noted swelling the size of walnut in the region of the urethra. The patient was married but had no children.

On examination the patient presented an oval, indurated mass, by 3 centimeters in size, with an ulcerated surface which bled easily located at the urethral opening on the anterior vaginal wall. In addition, both inguinal and femoral regions presented many hard lymph nodes.

On February 21, 1935, an excision of the urethral mass, including the anterior vaginal wall, and lymphadenectomy of the inguinal and femoral regions was performed. The wound healed but the patient became incontinent. She was discharged March 2, 1935.

Because of incontinence and deformity of the bladder, permanent suprapubic drainage was inserted on September 2, 1935. On July 29, 1936, an epithelioma of the clitoris which had been present for months was excised. On July 31, 1936 the vagina was contracted and the patient was able to control her urine.

On January 5, 1937, 4 years after the original operation, the patient died at Bellevue Hospital.

**Gross description** The gross specimen which included portions of the anterior vaginal wall, external meatus, and the tumor mass, measured 5 by 4.5 by 3 centimeters. An area of ulceration with undermined ragged edges and depressed base covered with coarse reddish nodules measuring 2 centimeters in diameter, completely surrounded the

urethra. The tumor mass appeared to invade the surrounding tissue but did not occlude the urethra. The mass of tissue removed from the right inguinal region contained fat and enlarged lymph nodes. The largest node measured 1.5 centimeters in diameter. The center of one of the nodes contained gross pus. The mass of tissue removed from the left inguinal region likewise contained fat and enlarged lymph nodes. The largest node measured 1.5 centimeters in diameter.

**Microscopic description.** The cells present a wide, solid, plexiform, card like arrangement. They are moderate in size, round to oval in shape, with a moderate variation in the size and shape. There is one mitosis per high power field. The cells are infiltrating and have a tendency to form pearls and keratin. The right inguinal node presents large clear round-oval cells which completely replace the normal lymph gland structure (Fig. 8).

**Diagnosis.** carcinoma with metastasis to the right inguinal nodes

### HISTOPATHOLOGY

The microscopic pathology of the 10 cases studied is variable but in all there is evidence of deep infiltration by small groups of cells arranged in clumps, sheets, or cords. The cells show a variation in their morphology and in some cases it is quite marked.

In 3 cases, P N 1819, 5879, and U N 38089, the cells have a tendency to form nodes, secrete mucin, and develop monster cells. In 2 cases, P N 2227 and 354, monster cells were formed, mucin secreted but no true glands formed. In 2 cases, P N 30375 and 37119, the cells simulated those of the bladder epithelium, in the latter case it is practically impossible to distinguish the cells from those of a bladder neoplasm. In 1 case, P N 10769, the cells showed extreme anaplasia, deep infiltration, and many mitoses. The cells in U N 25490 presented many mitotic figures and a moderate anaplasia.

In only 1 case, P N 20863, was there a definite squamous cell carcinoma with pearl and keratin formation.

### DIAGNOSIS

All tumefactions of the urethra and all chronic infections, not responding to treatment should be regarded as malignant lesions until proved otherwise. By this is meant that all tumefactions, regardless of their benign appearance and all suspicious lesions of the female urethra, should be subjected to a biopsy and microscopic examination. It is essential that biopsies be done in such cases, for signs and symptoms are so late and atypical that a microscopic examination is the only reliable method of diagnosis. Caruncles, urethral prolapse, and innocent looking papillary growths removed for various reasons should be studied microscopically after removal.

Carcinoma of the urethra may grow into a flat, pedunculated, or non-pedunculated lesion. Of the

10 cases studied, 7 were non-pedunculated, 2 pedunculated, and 1 flat. The outstanding signs on physical examination were

	Cases	Per cent
1 Induration	8	80
2 Ulceration	5	50
3 Bleeding on examination	4	40
4 Tenderness on examination.	4	40

No further attempt is made to describe the physical appearance of carcinoma of the urethra because the lesions are not typical except in the advanced state and even then a biopsy is necessary to verify an opinion.

Caruncles are usually recognized clinically by a smooth, red, non-indurated, tender growth usually located on the posterior lip of the urethra. They vary in size but are seldom larger than 1 centimeter in diameter.

Prolapsed urethras are continuous with the mucous membrane of the urethra. They are soft, non-tender, non-indurated, sometimes torn, and with no tendency to bleed.

In an effort to recognize early cases of carcinoma of the urethra, one might say that all women with urinary symptoms should receive a careful local urethral examination. In women who have reached the age of 40 years and who require periodical vaginal examinations of the cervix and uterus, should also receive a digital examination of the urethra with the vaginal examination.

In advanced cases the most important aids in clinical diagnosis are induration and a non-pedunculated mass. Helpful adjuncts in the diagnosis are ulceration and a tendency to bleed. Tenderness may or may not be present. Enlarged inguinal nodes when present are very suspicious and when proved metastatic are a hopeless sign.

### TREATMENT

Before treatment is instituted, a correct diagnosis by microscopic examination should be obtained. Many reports are present in the literature dealing with the treatment of carcinoma of the urethra, but they are conflicting in their results and as a whole are not encouraging.

A correct estimate of the value of various treatments is difficult in many cases for the follow-up reports are of too short a duration. Venot and Parcelier collected 30 cases treated by resection with a recurrence in only 5 cases. In this series, however, many were reported shortly after operation. At the end of 3 years, Crossen found that only 8 of 50 cases treated by resection of the urethra were free from recurrence. Mikulicz-Radecki advocates the local application of radium to primary growth and extirpation of the inguinal nodes

Counseller and Paterson consider that higher percentages of 3 year cures are obtained by radium and roentgen rays, although they report a case which is living 18 years after the lesion was first excised, cauterized, and later 232 milligram hours of radium applied. A second case was reported in which the patient was living 22 years after radium was applied to the lesion and X-rays applied to the inguinal region. Two separate applications of radium were made within a period of 2 years. Another case which received radium locally and roentgen rays over the inguinal regions was reported living 7 1/2 years later. The remainder of their cases, however show poor results, regardless of the treatment, whether it was irradiation, surgery or both.

Watson (25) reports no evidence of recurrence or metastasis following a wide excision of a carcinoma of the female urethra 20 years later.

Pomeroy reports a case free from recurrence and metastasis 9 years after the implantation of radium. However in 2 cases he reported deaths 3 months and 1 year respectively after the implantation of radium. Pomeroy uses heavily screened needles of low radium content and keeps them *in situ* for 2 weeks.

The results from the treatment in the present series are very poor. The best result was obtained in a 45 year old female who presented a fungating mass at the meatus and an inguinal metastasis. After the growth and the inguinal nodes were excised, the patient lived 39 months. Radium in the cases in which it was used produced no noted changes, although one case is under observation 4 months after the implantation with a reduction in the size and a marked decrease in the induration of the growth.

Dean does not advocate the use of radium in primary carcinomas of the urethra for the lesions are radioresistant and because the required dose produces a destruction of surrounding tissue, pain, and fibrosis. He, however advocates small doses of radium in the advanced cases as a palliative measure to decrease the size of the growth, reduce hemorrhage, and odor and to alleviate pain. In Dean's opinion, X-ray irradiation is useless in the inguinal region because the nodes are usually infected because of the preponderance of fat about the nodes, because the cells are radioresistant and because the skin will not tolerate a dose sufficiently great to produce any effect from the rays. Surgical removal in his opinion is the best method for treating metastatic lymph nodes once they are proved to be so, by aspiration biopsy. Prophylactic removal of the inguinal glands is unnecessary in Dean's opinion for he

considers the lymph nodes as nature's barrier to cancer. In the event that the lymph nodes are involved, he advises a rest of 3 months before any surgery is attempted, for during that period the associated infection present in the nodes has sufficient time to subside.

Watson (25) is in favor of a wide excision of the local lesion, surgical removal of both sets of inguinal nodes, and postoperative irradiation of the inguinal and urethral regions. Stout advises the surgical removal of both the local lesion and the inguinal glands. Lens believes that surgery is the treatment of choice in the majority of cases. However he believes that if the tumor cells are highly undifferentiated, such cases should be treated by applying radium to the lesion and irradiating the inguinal regions. In growths showing differentiated tumor cells, the best treatment is surgical removal of the growth and inguinal nodes.

Wood believes that all cases should be individualized and that no generalities should be made in regard to the treatment of carcinoma of the urethra. He, however is of the impression that surgery is indicated in the majority of cases.

Although scattered reports of cures of carcinoma of the female urethra by surgery, radium, or both, are found, the treatment by any method is highly unsatisfactory in the majority of cases.

Judging from the results in the literature, the results in the present series, and from the various opinions expressed on the treatment of carcinoma of the female urethra, it is believed that the best results are obtained by radical extirpation of growths which are not too extensive and in which complete removal is possible. The cases best suited for surgery are those in which the growths are limited to the anterior urethra. It is also believed that the inguinal nodes should be removed surgically. When the growths are extensive and beyond the possibility of complete extirpation, they are probably best treated by small, and if necessary, repeated doses of radium and X-ray.

#### PROGNOSIS

The prognosis of carcinoma of the female urethra, regardless of the treatment, is poor. The late stages in which the majority of the lesions are first discovered the infiltrating tendency of the growth, and the apparent radioresistance of the lesions are the outstanding factors responsible for the poor prognosis.

Ehrendorfer and Shaw are of the opinion that inguinal glands are involved in one-third of the cases. Three of the present 10 cases showed evidence of metastasis.

## SARCOMA

Sarcomata of the female urethra are rare. In 1931, Thurn-Rumbach found 19 cases in the literature and reported a separate case. He, however, made no mention of the cases of Hirst and Mundel. Among the types reported in the literature are a round cell sarcoma by Beigel in 1875, a myxofibrosarcoma by Hallervorden in 1896, a spindle cell sarcoma by Serenus in 1909, a melanotic sarcoma by Reed in 1896, and a myxosarcoma by Watson (26) in 1914.

Sarcomata may arise from any of the supportive structures of the urethra. It is also possible for sarcomata to arise from nerve tissue supplying the urethra.

The method of arriving at a correct diagnosis in sarcomata is similar to that mentioned in carcinomata, i.e., biopsy. Before any treatment is instituted, the radiosensitivity of the tumor should be determined. In radiosensitive sarcomata, radium should be used.

The following case is presented here because it is impossible definitely to state whether the lesion is a sarcoma or a carcinoma.

U N 56193 (Dr G W Fish). A white female, 57 years of age, was admitted to the Squier Urological service on October 13, 1932, complaining of pain in the bladder for 4 months, a frequency, a nocturia, and a loss of control of micturition. Five years previously, following an intermittent hematuria, the patient received a cystoscopic fulguration of a bladder tumor. Following this, the patient received fourteen cystoscopic fulgurations. She appeared obese but a physical examination was entirely negative. Cystoscopic examination revealed a small papilloma above the left ureteral orifice. The papilloma was fulgurated and the patient was discharged on October 15, 1932.

On February 14, 1933, she was readmitted for a cutting pain in the vagina. She also complained of hematuria for 3 weeks, bleeding from the urethra, frequency, urgency, dysuria, nocturia, and an interruption in the flow of urine. A cystoscopic examination revealed a bleeding papilloma located to the left of the internal sphincter and a papilloma lateral to the left ureteral orifice. Both papillomata were fulgurated. The patient was discharged on February 15, 1933.

On May 13, 1933, a cystoscopic examination revealed a posterior urethra which appeared involved by a non specific posterior urethritis. Silver nitrate was applied locally. The urethra on vaginal examination was indurated.

On June 14, 1933, the patient was admitted for a gross intermittent hematuria, a frequency, and a nocturia. Vaginal examination revealed an induration along the urethra, 5 centimeters in length and 2 centimeters in breadth. The induration was larger than that noted on May 15, 1933. A cystoscopic examination revealed hemorrhagic areas about the trigone and a fimbriated tumor surrounding and projecting from the left ureteral orifice. Urethroscopy revealed a urethra which bled easily. The posterior urethra presented a markedly injected area extending to the bladder neck. A biopsy was made of the posterior urethra.

On June 23, 1933, 8 tubes of radium (1 millimeter platinum filter) each containing 12.5 milligrams were inserted

through the anterior wall of the vagina around the floor of the urethra. The tubes were removed after 25 hours. The total dosage was therefore 2,500 milligram hours.

On June 27, 1933, there was edema of the clitoris and labia minora. The patient was sent home for a rest on July 8, 1933.

On August 3, 1933, the patient was readmitted for X-ray irradiation. On examination, the lesion was found to be firmer but there was no decrease in the size of the growth. X-ray irradiation. From August 3, 1933, to August 21, 1933, patient received sixteen X-ray treatments, each consisting of 132 milliamperes minutes, directed in the region of the urethra, alternately using anterior, posterior, and perineal exposures.

On August 19, 1933, the gluteal regions presented a pale pink erythema. A mild erythema was also present over the thighs anteriorly. On August 23, 1933, the patient complained of rectal pain and tenesmus. The urethra bled when palpated. On August 26, 1933, she passed sloughed mucous membrane from the rectum. The perineal, thigh, and gluteal regions presented marked excoriations. Palliative measures and a diet of toast, tea, broth, and ginger ale relieved the patient of the rectal symptoms.

The patient died in February, 1934, 8 months after the radium implantation, suffering from deep ulcerations in the gluteal thigh and urethral regions. She had suffered from much pain.

**Microscopic description.** The cells grew diffusely but for the most part were arranged in bands which had a tendency to interlace (Fig 9). The growth was characterized by the formation of spindle cells. The cytoplasm was acidophilic. There was a moderate variation in the size and shape of the cells. There was no evidence of keratin, intercellular bridges, pearls, mucin or myofibrils. It might be an epithelioma because it is known that some undifferentiated epitheliomata grow in a spindle cell form. In some areas the tissue appeared to be a spindle cell sarcoma, while in other areas the tissue resembled a spindle cell metaplasia. Since there was no further differentiation, it is impossible to state whether the lesion was a sarcoma or a carcinoma.

## SUMMARY

1 Ten cases of carcinoma of the female urethra are presented, together with a general study of the disease as a whole.

2 A case in which it is impossible to state definitely whether the lesion is a sarcoma or a carcinoma is presented.

I wish to express my gratitude to Dr F Carter Wood for his advice and criticism, to Dr A. P. Stout for his advice and criticism, and to the surgeons who kindly permitted me to study and publish the cases reported in this article.

## BIBLIOGRAPHY

- 1 BEIGEL, H. Mitteilung vom Jahre 1875—Krankheiten des weiblichen Geschlechtes. 1875, 2 653.
- 2 BOVIN, M A V G, and DUGÈS, A. Traité pratique des maladies de l'utérus et de les annexes p 648. Paris, 1883.
- 3 COUNSELLER, V S, and PATERSON, S J. Carcinoma of the female urethra. J Urol, 1933, 29 587-595.
- 4 CROSSEN, H. S. Med Rec., 1915, 88:418 (Quoted by Shaw, 20).
- 5 DEAN, A. L. Personal communication. Memorial Hospital, New York City.
- 6 EHRENDORFER, E. Ueber Krebs der weiblichen Harnroehre. Arch f Gynaek., 1899, 58:463-491.

- 7 ENGLISH, J. Folia urolog. 007 6 57
- 8 HALLER-ORDEN. Inaugural Dissertation, Greifswald, 866. (Quoted by Thurn-Kambsch, 3)
- 9 HIRST, B. C. Tumors of the urethra in women, with special reference to malignant growths. Am. J. Surg., 000, 21 383-39
- 10 LIND, M. Personal communication. Presbyterian Hospital, New York City
- 11 MONTAGNIER-KAPSCHEK, F. V. Zur Behandlung der Urethralcarcinome. Zentralbl. f. Gynaek., 193 23.20 3-2015
- 12 MONROE, D. E. Melanosarcoma of the female urethra. Kingston Med Quart. 007-008, 5 75
- 13 PALMER, A. C. Carcinoma of female urethra, treated by partial resection of urethra. Proc. Roy. Soc. Med. 022, 8 (Sect. Obst. & Gynec.), 45-47
- 14 PRATT, J. L. Primary carcinoma of the urethra in the female. Am. J. Obst. & Gynec., 008, 47 457-458
- 15 POWERS, L. A. Three cases of primary carcinoma of the female urethra treated with radium. Am. J. Obst. & Gynec. 1934, 27 606
- 16 REED, C. A. D. Melanosarcoma of the female urethra, urethrectomy, recovery. Am. J. Obst. & Gynec. 308, 34 864-867
- 17 ROCHETTE, H. Anatomie des lymphatiques de l'utérus 93 pp 34 35
- 18 SCHWELL, A. J. JR., and BALLANCE, W. T. Primary tumors of the urethra. Ann. Surg. 022, 76 246-30
- 19 SCHWELL, Zentralbl. f. Gynaek. 007, p. 2007 (Quoted by Thurn-Kambsch, loc. cit.)
- 20 SEE, W. W. F. Carcinoma of the female urethra with notes of two cases treated with radium. J. Obst. & Gynec. Brit. Emp. 023, 30 35
- 21 STOUT, A. P. Human Cancer p. 395 Philadelphia Lea & Febiger 03
- 22 Idem. Personal communication. Presbyterian Hospital, New York City
- 23 TURNER-ROBERTSON, S. V. Ueber das Sarkom der weiblichen Harnroehre. Ztschr. f. urol. Chir. 03 35. 215 5
- 24 VENOY, A. and FACHELIER, A. Le cancer de l'urètre chez la femme. Rev. de chir. 9 1, 89 563
- 25 WATSON, B. P. Personal communication. New York City
- 26 Idem. Primary malignant tumors of the urethra in the female. Am. J. Obst. & Gynec. 014, 49 797-806
- 27 WINTERBOURN, B. Primary carcinoma of the female urethra. Proc. Roy. Soc. Med., 0 5 (Obst. sect.), 24-26
- 28 WOOD, F. C. Personal communication. New York City

KNEE FLEXION CONTRACTURE TREATED BY SKELETAL TRACTION<sup>1</sup>

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**F**LEXION contracture of the knee joints, regardless of degree, causes disability. In the severe type of this deformity, the patient is confined to bed or chair, because, in attempting to assume the upright position, the flexed knees force flexion in turn at the hip joint, that is, trunk on thigh, in order to maintain body balance (Fig 1). Even to suppose the joints themselves were painless, walking any distance in this position is wellnigh impossible because of fatigue.

Furthermore, flexion contracture of the knee joints is a relatively frequent deformity—due to various causes which are briefly outlined below. It is believed that treatment of this contracture by skeletal traction in the line of the deformity is one of the simplest and at the same time most effective procedures to correct many of these cases of persistent knee flexion. With this technique it is possible to utilize continued physiotherapy and active muscle exercises throughout the interim of treatment, and thus appreciably shorten the period that the patient must remain under active supervision.

In certain of the more severe cases (grade 2 contracture) skeletal traction is supplemented by lengthening of the biceps tendon and division of the iliotibial band and lateral intramuscular septum.

In a third group, fortunately not common (grade 3 contracture), the persistence of the deformity is due to changes in the posterior capsule as described by Silver. In these cases skeletal traction is inadequate. The only effective treatment is to attack the capsule surgically—as accomplished in the capsuloplasties of Silver or of Wilson.

## CLASSIFICATION

The types of flexion contracture of the knee joint are grouped as follows:

**Arthrogenic.** The result of disturbance in the joint itself, best illustrated by the deformity seen in atrophic or rheumatoid arthritis. The majority of knee joint contractures fall in this group.

**Neurogenic.** In which the "fixation is brought about by contraction of a muscle or muscle group as a result of abnormal innervation" (Foerster).

**Myogenic.** (A) Paralytic—the result of muscular imbalance as in poliomyelitis. (B) Myostic

—the result of inflammatory processes in the adjacent muscles, notably the hamstring group.

**Congenital.** Usually associated with flexion contractures elsewhere in the body as in the fingers, elbow joints, hip joints, and so forth.

**Static.** Consequent upon hip flexion, short gastrocnemius, or from faulty posture.

With the exception of neurogenic contractures, cases in all the above groups have been treated by the method herein described.

Considering all forms of knee flexion contracture, it is at once obvious that certain cases are not amenable to the skeletal traction type of treatment. In this group is knee flexion from a mechanical cause, such as internal joint derangement due, for example, to a fractured and displaced semilunar cartilage, posterior capsule contracture, already mentioned, acutely inflamed knee joint, and knee contracture, the result of extensive soft part injury, as in burns.

## METHODS OF TREATMENT

In knee flexion deformity from the causes described, diverse methods of treatment have been advised. The literature contains numerous references to varied forms of mechanical appliances, such as described by Schaffer, Goldthwait, Smith, Campbell, and Lord. Results have been achieved with each type of apparatus.

One of the more commonly employed methods is that of the wedging plaster cast. Figure 2 illustrates the mechanism of this type of treatment. The cast is applied to the limb without attempting correction and then a wedge cut out over the knee. The remainder of the plaster is divided posteriorly at the same level and the lower leg then progressively forced into extension. When correction is obtained the plaster cast is completed. The wedge actually should be cut in the form of a U (Fig 3), convex distally in such a manner that the apex of the U fits down over the anterior aspect of the patella and thus protects it, as well as offering a much more effective point against which to exert the force applied in the correction of the flexion deformity.

There are several disadvantages to the wedging cast. Unless considerable care is exercised, subluxation of the tibia is prone to occur, particularly where the flexion deformity is pronounced. Fur-

<sup>1</sup>Presented before the American Academy of Orthopedic Surgeons, New York, January 14, 1935.



therefore, in long standing cases of this deformity because of the marked loss of muscle tone and the atrophy that is present, a wedging plaster should be utilized with caution. To encase the already atrophied extremity in plaster makes still further muscle atrophy inevitable and hence prolongs disability. While in the presence of the atrophic bones so commonly found in these cases, fracture is an ever present possibility.

If plaster treatment is decided upon, the turn buckle cast is decidedly superior to the wedging cast. In our experience this method has been particularly efficient in elbow contractures. At the knee joint with the turnbuckle placed posteriorly it is progressively more difficult to overcome resistance as correction of the deformity proceeds, because the angle of application of the correcting force becomes progressively less. Kulowski meets this contingency by placing the turn buckles anteriorly, fixed to uprights incorporated in the cast. His reports excellent results with this method.

In a rigid system, as provided by the plaster casts described, powerful leverage can be applied when the forces are correctly aligned to overcome knee flexion contracture. On the other hand, use of a cast precludes any attempt during correction to apply physiotherapy and muscle exercises, while with skeletal traction the opposite is true, namely that physiotherapy is instituted at the onset of treatment. In our observation early massage and active exercise of the leg muscles is decidedly a factor in hastening recovery.

A not inconsiderable advantage of the plaster is that the patient can shortly become ambulatory in the cast. However in our experience with skeletal traction, the total time of continuous bed confinement has not exceeded 3 weeks—the average is 2 weeks. Since the patient can assume an upright sitting position in bed during treatment and also perform active exercises, no ill results have developed, while from the general functional standpoint, a period of bed rest has often been very beneficial.

A successful surgical procedure in the treatment of these cases is that of Wilson's so called posterior capsuloplasty. In this operation the capsule of the knee joint is stripped under direct exposure from the posterior aspect of the femur and the leg then brought into full extension. Wilson also divides the iliotibial band, and lengthens the biceps tendon. It should be kept in mind, however that when this operation is performed in cases of chronic arthritis it is absolutely essential that the arthritic process in the knee joints be quiescent. If this joint reaction has not been en-

tirely controlled when the operation is done, a marked increase in the activity of the arthritis may follow which in turn can result in fixation of the knee in the position of full extension with pronounced disability. To obtain adequate control of such an arthritis may require a considerable period of time often many months. For the average patient such a period of hospitalization is extremely difficult, at times impossible.

Skeletal traction in the line of the deformity provides an effective and, at the same time, a simple method of correcting knee flexion contractures. Anyone having experience in the treatment of fractures of both bones of the lower leg by skeletal traction will have many times employed the traction as herein described. It is believed that the efficacy of this type of traction in the treatment of knee flexion deformity is not widely appreciated, particularly now that wire traction has largely superseded the use of pins and tongs. In certain cases of pronounced knee flexion of long duration and marked soft part contracture the skeletal traction is supplemented by division of the iliotibial band, the lateral intramuscular septum, and lengthening of the hamstring tendons, notably that of the biceps (see below).

*Technique of skeletal traction in knee flexion deformity.* The patient is usually given a general anesthetic—evarts preferred—to eliminate all voluntary muscle pull and so permit an accurate estimate of the degree of the deformity and its resistance to correction. Under careful asepsis a Kirschner wire is then passed through the upper anterior tibial cortex as shown in Figure 4. A second wire is directed through the os calcis or if the flexion deformity is marked, then through the lower end of the tibia (Fig. 4). The extremity is supported in a Thomas splint with a Person hinged knee attachment (Fig. 5) and traction then exerted in the line of the deformity. The degree of the traction naturally depends upon the estimated resistance to correction. The average amount of weight attached to the lower wire in adults varies from 6 to 18 pounds. For the upper wire the weight averages from 3 to 7 pounds.

The wire through the upper tibia prevents posterior displacement or subluxation of that bone and also acts as a traction force in amplifying the main traction pull exerted in the lower tibia or in the os calcis. In none of the cases treated has tibial subluxation occurred.

It is important to note, as shown in Figure 4, that the bow holding the wire in the lower end of tibia is of sufficient size so that as the leg goes

into extension the foot may pass through the bow

On obtaining extension at the knee of 160 to 170 degrees, skeletal traction is removed from the lower tibia and then reapplied through the os calcis (Fig 6) With the traction force at this latter point, the remaining degree of knee flexion deformity is then corrected Not only is traction still applied to the muscles of the posterior thigh, but also, by means of the pull through the os calcis shortening of the calf musculature is overcome, an important part of the deforming elements in a flexion contracture of the knee

During this period of traction which, in the cases here reported, varied from 10 to 18 days, frequent leg massage is given combined with radiant light and active exercises in the splint On removal of traction, the leg is supported in a posterior plaster splint running from the gluteal fold down to the ankle Thereafter, a caliper brace is fashioned which, after application, is at first worn continuously but later only at night With the application of the caliper splint the patient becomes ambulatory and begins progressive walking with crutches, increasing his activities as the muscle power improves Gradually, the splint is discarded during the day but it is worn at night for the ensuing 3 to 6 months, depending on the degree of resistance encountered in correction of the contracture

In knee joint contracture due to hip flexion, the patient is placed on a convex Bradford frame (Fig 7) and traction instituted Both deformities may be corrected in this manner

*Operation supplementing skeletal traction* If the flexion contracture is very pronounced, for

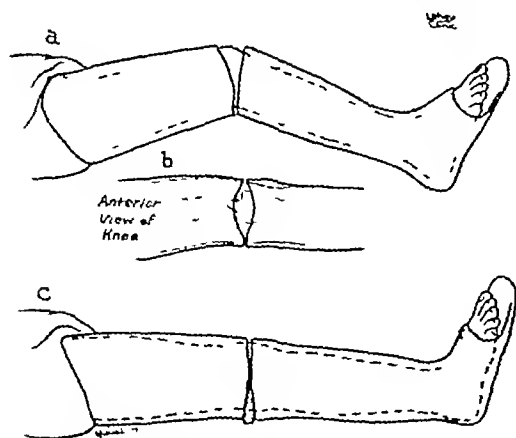


Fig 2 Line drawing to illustrate application of wedging plaster cast for correction of knee flexion deformity



Fig 1 Photograph of patient with bilateral knee flexion contracture illustrating faulty body mechanics resulting from this deformity

example, the maximum extension at knee joint is a right angle, or if the contracture while not so severe is of long duration, then skeletal traction is supplemented by open operation

The surgical attack is directed (1) against those structures which are particularly resistant to correction, viz, the tendons of the hamstring muscles, especially the biceps tendon, the iliotibial band, and the lateral intramuscular septum, (2) to prevent a stretching injury of the common peroneal nerve

The operative approach is that described by Henry for lateral exposure of the popliteal space An incision 6 inches long (Fig 8) is made at the inferior margin of the iliotibial band and extends

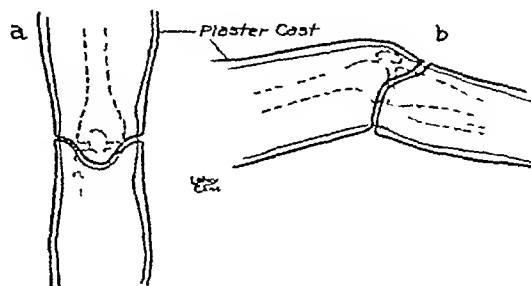


Fig 3 Preferred method of cutting wedging plaster cast for knee flexion deformity note U shaped extension of plaster protecting patella

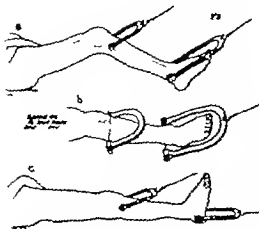


Fig. 4. Illustrating progressive steps in application of skeletal traction for correction of knee flexion deformity. When traction is applied to lower tube, note that bow is sufficiently large to permit foot passing through it as the knee joint extends.

across the line of the knee joint to beyond the head of the fibula. Following division of the deep fascia, blunt dissection posteriorly behind the margin of the biceps muscle easily reveals the large common peroneal nerve which is then traced distally and exposed as it bifurcates upon the neck of the fibula where the nerve trunk pierces the substance of the peroneus longus muscle. The latter muscle and the overlying fascia are divided horizontally as illustrated in Figure 9. This simple maneuver permits forward displacement of the nerve when the knee joint is fully extended and thus prevents loss of nerve function due to constriction of the nerve trunk against the muscle and fascia—a constriction which otherwise frequently occurs in the correction of severe flexion deformities of the knee. None of the patient operated upon has experienced disturbance in the peroneal nerve as a result of correction of the knee flexion contracture.

The iliotibial band is next defined and then divided by excision of a segment, 2 inches in length (Fig. 10, a). The posterior margin of this band is continuous with the lateral intra-

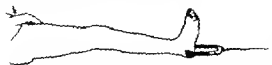


Fig. 6. Skeletal traction through os calcis applied following removal of traction through upper and lower tube. Traction on hamstring muscles is then continued and complete correction obtained of calf muscle shortening.



Fig. 5. Lower extremity in Thomas splint suspended in Persson shaped knee attachment. Active extension of the muscles are then permitted while skeletal traction is correcting knee flexion deformity.

muscular septum. Therefore by lateral reflection of this segment a similar area of the septum is easily visualized and removed down to the bone (Fig. 10, b). The significance of the lateral intramuscular septum in hip flexion has been emphasized by Nicbet. Fixation of this septum may also be a factor in the persistence of knee flexion contracture. In 2 of the author's recent cases, it was necessary to strip up the septum from distal half of femur before full extension of knee joint was secured.

Finally the biceps tendon is isolated and then lengthened either by Z shaped incision or by the Hildebrand tenotomy (Fig. 11).

Division of the iliotibial band and septum plus lengthening of the biceps tendon is of particular significance in these cases, because the tensor fasciae femoris and the biceps femoris are external rotators of the knee joint and tend to increase the valgus deformity so often present in these flexion contractures. By the procedure described, this deforming effect is eliminated.

In closing the incision, experience has shown that it is unwise to suture the deep fascia directly over the lateral aspect of the knee joint region, because the common peroneal nerve, now displaced anteriorly may be caught in the scar and nerve function impaired. This happened in 1 case of a congenital flexion contracture treated



Fig. 7. Lane drawing to illustrate use of convex Bradford frame for combined correction of knee and hip flexion deformity.



Fig 8 Illustration to show incision for exposing common peroneal nerve, biceps tendon, iliotibial band, and lateral intramuscular septum (From Henry)

by wedging plasters and operation. A secondary operation to free the nerve was later necessary.

#### RESULTS

Skeletal traction for correction of knee flexion contracture has been carried out a total number of eighteen times in 12 patients. There was a bilateral flexion deformity in 6 patients. Open operation, as described, was performed on 7 knees.

The longest follow up is 3 years, the shortest 6 months. Three patients are now under active supervision, hence are not included in the above group. The result of these procedures has been most encouraging. With 1 exception (see case reports) all the patients have maintained correction of the pre-existing knee flexion, while remaining ambulatory. There is no instance of tibial subluxation in this group.

#### SUMMARY

A classification of types of knee joint flexion contracture (excluding mechanical cause) is presented. The frequent occurrence of this deformity is stressed.

Methods of treatment are briefly reviewed. The use of skeletal traction is advocated because of its effectiveness, simplicity, and ease of application.

In either long standing or pronounced knee joint contractures, skeletal traction may be supplemented by division of the iliotibial band, lateral intramuscular septum, and the lengthening of the biceps tendon. By this operation the tendency to valgus deformity and external rotation of the knee is eliminated, and recovery is hastened.

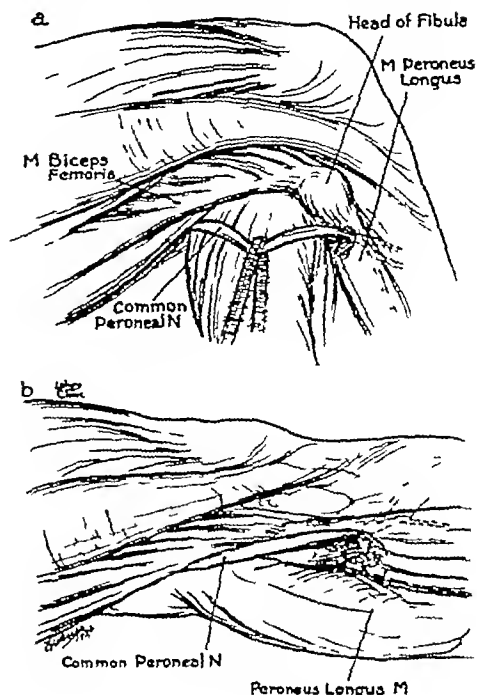


Fig 9 Dissection of common peroneal nerve. Division of soft parts in region over neck of fibula to prevent constriction of nerve following correction of knee flexion contracture.

In these severe cases, it is important to permit anterior displacement of the common peroneal nerve by dividing the soft parts directly lateral and anterior to the neck of the fibula. Constriction and stretching of the nerve, with consequent muscle weakness or even paralysis, is thus prevented following correction of the knee flexion deformity.

#### CASE REPORTS

The following cases are reported in detail to illustrate the type of knee flexion contracture treated by the procedure described and further to illustrate the details and the steps of this treatment. The findings of the complete examination, the diet, and the various forms of therapy are omitted to save space. It is understood, however, that all of these patients had a very complete general and local examination followed in turn by the institution of those measures which seemed best indicated to aid the individual problem presented.

**CASE 1** Mr. James S., aged 46 years, mill hand. Diagnosis: chronic multiple rheumatic arthritis. Pronounced bilateral flexion contracture of knee joints with marked disability following

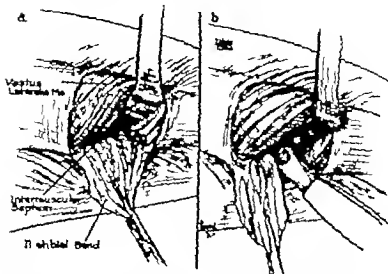


Fig. 2. Extent of segment of the tibial band and division of lateral intramuscular septum.

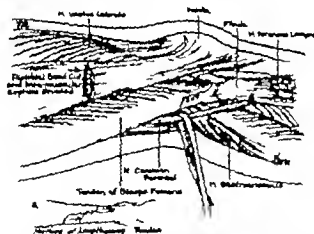


Fig. 3. A composite view of the various steps in the supplementary open operation for correction of severe flexion contracture of the knee joint, dividing the ilio-tibial band, with division of soft parts over region of fibula to neck of tibia to prevent nerve constriction, division of the tibial band and the lateral intramuscular septum, lengthening of biceps tendon.

The procedure followed in this case was not exactly the one employed, but review of the course of this patient well illustrates the effectiveness of skeletal traction as the reduction of knee flexion deformity. This patient falls in the group of grade 4 contractures in which there is definite thickening, scarring, and contracture of the capsule of the joint. Capsulotomy the preferred therapy for this type of case, was not considered in this instance because the arthritis as so active that any attempt, such as operation, would be been disastrous. Furthermore it was not

possible to keep this patient in the hospital long enough to carry out time-consuming quiescence of the arthritis.

June 5, 22 Patient was admitted to the clinic complaining of extreme atrophic arthritis involving all the major joints of the body and particularly of pain and loss of function in the knee joints. The latter condition, as of 1 year's duration, had rapidly and progressively become worse so that for the past 3 years he had been unable to walk farther than a few steps across his bedroom. Examination of the knee joints revealed bilateral flexion de-



Fig 12, a and b Case 1 Photograph of recurrent flexion contracture of knee before and after correction by skeletal traction

formity in which the maximum extension was 5 degrees beyond a right angle. Both knee joints were swollen and contained a large amount of fluid. His general condition was very poor. There was a pronounced generalized muscle atrophy, marked secondary anemia, and a very inadequate gastro intestinal function.

As it was not possible for patient to enter the hospital at this time, following a preliminary investigation, he was sent home with dietary instructions and advice to relieve stress and strain on the joints, particularly the knees.

August 30, 1931. He was admitted to the hospital. Flexion contracture was as originally described. Patient had not carried out instructions given but instead had continued to attempt walking. Under ethylene anesthesia, the joints were gently manipulated and wedging plasters applied with appreciable degree of correction of flexion deformity. Ten days later, the procedure was repeated. Complete correction of the deformity in the left knee and on the right side within 3 to 5 degrees of full extension.

September 4, 1931. Bilateral division of iliotibial bands and lengthening of biceps tendon. Construction of the common peroneal nerve was seen at operation, on full extension of the knee, and therefore the procedure described to relieve this constriction was carried out.

October 14, 1931. Patient refused to purchase caliper braces as he was so pleased with his progress that he felt braces not necessary. He did agree to walk with crutches. Muscle power was exceedingly poor. At this time patient had a full 180 degrees' extension in the right knee, with flexion to 10 degrees less than a right angle. On the left side the range of motion was from a full 180 degrees' extension to a flexion of 6 degrees short of a right angle. Discharged.

October 15, 1932. 13 months since first institution of treatment. Patient was seen very irregularly during this interval. He was walking with crutches, and was quite pleased with progress. There was a definite recurrence of flexion deformity in both knees. The maximum extension on the left was to 170 degrees, and on the right to 160 degrees. He declined further treatment at this time.

September 4, 1933. Patient returned and requested admission to the hospital, as flexion contracture was increasing. He was able to walk much better than when first seen. He had not carried out exercises as directed nor had he worn any retentive appliance. As patient could not remain in the hospital long enough to quiet down the process, and as both knees showed a considerable amount of fluid indicating a very active process, skeletal traction was therefore advised. There was a bilateral 20 to 25 degrees of knee flexion deformity.

Skeletal traction was instituted on this date with a wire through the os calcis and the upper tibia of the right leg and through the os calcis of the left. Ninety cubic centimeters of cloudy yellow fluid was aspirated from both joints. The bacteriology of this fluid was again negative. Complete extension of both knee joints without evidence of tibial subluxation by X-ray was obtained in 10 days following onset of this traction. He was then fitted with caliper braces

and began walking again with crutches. Figure 12, a and b photographs of the left knee taken with the patient lying supine, before and after correction of the deformity by skeletal traction.

August 1, 1934. Patient returned again for follow up examination. Full extension had been maintained. Flexion in left leg was to right angle, in the right knee to 3 to 5 degrees beyond a right angle. He continued to wear caliper braces intermittently. Muscle function was still very poor. He was advised to continue with crutches.

Bilateral grade 3 contracture of knee joint in a patient exhibiting advanced atrophic arthritis who has co-operated very poorly. In spite of the degree and type of the deformity, skeletal traction was successful in correcting the flexion at the knee joint within 19 days time following the onset of traction.

CASE 2 Mrs. Grace C. aged 56 years, housewife.

Diagnosis: chronic multiple atrophic arthritis with pronounced bilateral flexion deformity of knee joint of 2 years' duration.

August 9, 1932. Patient was admitted to the clinic with chief complaint of inability to walk because of pain in the knee joints. She had been unable to extend the right knee fully for over 2 years and the left knee about 1 year. She was able to get about bedroom only with the aid of canes. Figure 13 is a photograph of patient on admission. At this time she was unable to stand even with the aid of canes unless two people supported her.

On examination patient presented evidence of considerable loss of weight, marked secondary anemia, bilateral flexion contracture of both knee joints. On the right the maximum extension was 10 degrees beyond a right angle. On the left a maximum extension of 30 degrees beyond a right angle. Maximum flexion was 10 to 12 degrees less than a right angle in each knee joint. There was marked atrophy and wasting of musculature of the body as a whole and particularly of the lower extremities.

October 14, 1932. Under avertin anesthesia skeletal traction was instituted, as described, to both lower extremities. Because of patient's poor condition operative measures were not considered. One week later there was a maximum extension of left knee to 175 degrees, and on the right between 165 and 170 degrees. General condition was good. At this time wires from the upper end of each tibia were removed.

October 28, 1932. Complete extension of both knee joints was obtained. Patient could easily flex both knees to a right angle in apparatus.

November 10, 1932. 27 days since institution of traction. Patient walked in caliper braces (Fig. 14). Braces were removed four times daily and patient carried out active exercises following intensive physiotherapy in the form of massage and radiant light. Active range of motion in



Fig. 14. left Case. Photograph of patient on admission. Unable to stand unless supported by two assistants.

Fig. 14. Case. Photograph following correction of deformity by skeletal traction. Patient wearing caliper braces.

each knee joint was from full 250 degrees' extension to right angle in the right knee, and to degrees less than right angle in the left knee.

December 17, 1932. Discharged. Note: Patient remained in hospital for period of months because she came from Florida and had no relatives or family adjacent to Boston.)

August, 1934. Figure 5, a, b, and c, photographs showing the patient's condition at the present time. The flexion deformity of the knee remains corrected, and the patient has flexion range to right angle in each knee. I feel that this degree of motion could have been appreciably increased if patient were under our active supervision.

Bilateral, grade 2 arthritic knee flexion contracture of 3 years' duration in a poorly nourished and emaciated woman of 60. Correction of deformity was accomplished in 2 weeks by skeletal traction. Two years follow up shows normal extension of both knee joints and flexion to a right angle.

Case 3. Miss Laura B., aged 27 years, school teacher. Diagnosis: pronounced flexion contracture (static) of right knee joint and of right hip joint (myostatic) 3 months' duration. Chronic suppurative osteomyelitis of the lumbar spine (third and fourth lumbar vertebrae), a large abscess in right psoas muscle. Septicemic. Malnutrition, wasted.

March 5, 1933. Patient was admitted to clinic complaining of inability to move the right leg and of severe pain in the right lower back. The symptoms dated 6 months previously from carbuncle on the back of the neck which had improved after being incised and poulticed. At that time, however, she developed sudden onset of severe pain in the right low back and hip regions which persisted until the present. With onset of back pain, the leg began to draw up and remained in this position. Figure 16 illustrates the maximum amount of extension in the right hip and knee joint on admission. Various methods of treatment had been tried elsewhere without success.

On examination the patient, as found to be obviously extremely sick. Blood culture positive for *Staphylococcus aureus* temperature 104 degrees, fixation of knee and hip as illustrated. There is severe fullness in the right flank and costovertebral angle and marked pain on palpation over the midlumbar space. X-ray films revealed suppurative osteomyelitis involving the posterior elements of the third and fourth lumbar vertebrae. Prominent muscle spasm was noted over the right flank and loin and indicated a postperitoneal abscess. On March 9 operation revealed large abscess cavity extending well down into the iliac fossa and in the substance of the psoas muscle. There was no evidence of peritoneal infection.

April 1, 1933. Drainage of osteomyelitis of the lumbar spine. Multiple small sequestra removed. Extensive destruction was found of apophyseal processes and right laminae and pedicles of the third lumbar vertebra and to slightly less extent of the fourth lumbar vertebra. A vesicle gauze pack, as inserted and a body plaster cast was applied.

April 1, 1933. Her general condition was greatly improved. Temperature now ranged between 99 and 100 degrees. Flexion deformity remained as 1 entrance. Under vertebra anesthesia, plaster jacket was again applied following change of dressing and the rods of special Thomas splint were incorporated in the jacket which was extended down as short space as just above the left knee to immobilize the pelvis. (The author is indebted to Dr. S. M. Fitchet for valuable suggestions in working out details of this apparatus.) Skeletal traction



Fig. 15. b and Case. End result 2 years later. Now maintenance of correction of deformity. Motion of knee joints to right angle.



Fig 16

Fig 16 Case 3 Photograph on admission showing maximum extension of right knee and hip joint

Fig 17 Case 3 Photograph of patient in apparatus Skeletal traction to upper and lower tibiae beginning correction



Fig 17



Fig 18a

Fig 18b

Fig 18, a and b Case 3 Follow up result, 2 years and 6 months after treatment Correction of severe right hip and knee flexion has been accomplished Patient has resumed normal activities, and she presents no symptoms

instituted by wire through upper and lower right tibia as shown in Figure 17

May 6, 1932 Complete correction of flexion deformity of right hip and knee was obtained, total duration of traction, 3 weeks Discharge from the granulating wound over the spine still was profuse but the wound was gradually closing in It was necessary to keep patient in a body jacket to prevent crushing down of the spine and as patient's finances were such she desired to visit home, a right plaster hip spica was applied with right knee and hip maintained in a position of full extension Patient discharged and treatment temporarily stopped

June 3, 1932 Patient returned in excellent general condition The plaster was changed over the body and a walking caliper was applied to the lower right extremity Patient then again discharged home to carry out exercises

September 30, 1932 She returned for check up examination Figure 18 a and b, shows complete correction of knee flexion deformity and with good muscle balance of extremities Patient walked normally

August 1, 1934 Since above note she has had no further complaint X ray films of the spine show complete regeneration of the destroyed bone No deformity There is normal motion in both hip and knee joints For the past 19 months patient has resumed her usual activities and occupation

Patient, a young woman of 27, had a very pronounced flexion contracture of right hip (mosaic) and of right knee (static) originally caused by a suppurative osteomyelitis of the lumbar spine with large postperitoneal abscess involving psoas muscle, positive blood culture Following drainage of abscess and of osteomyelitis of spine, flexion deformities were corrected by skeletal traction in 3 weeks

Follow up 2 years and 6 months later shows normal motion and function in hip and knee joints with preservation of normal X-ray appearance of the spine

CASE 4 Miss Elizabeth C, aged 17 years schoolgirl Diagnosis flexion contracture right knee joint, 5 years' duration Ulcer of right knee region, 5 years' duration Old healed severe burns of both lower extremities

The persistent ulceration in the region of the knee and loss of function of this joint was the result of a severe burn of both lower extremities sustained 8 years previously Many grafts of various types had been applied elsewhere All had healed and epithelization was complete except for an area over the anterior inferior aspect of the right knee region where there was a dirty granulating wound measur



Fig 19a.

Fig 20a.



Fig 19b

Fig 20b

Fig 19, a and b Case 4 Photograph of patient on admission

Fig 20, a and b Case 4. Follow up result, 11 months Complete correction of deformity and usual activities No symptoms



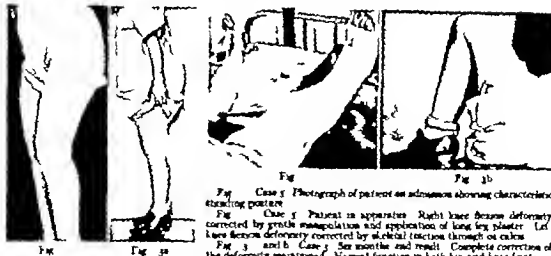


Fig. 1 Case 5. Photograph of patient on admission showing characteristic straddling posture.

Fig. 2 Case 5. Patient in apparatus. Right knee flexion deformity corrected by gentle manipulation and application of long leg plaster. Left knee flexion deformity corrected by skeletal traction through os calcis.

Fig. 3 and 4 Case 5. Six months' end result. Complete correction of the deformity maintained. Normal function in both hip and knee joints.

ing about 3 by 4 inches. There was flexion deformity of 5 degrees at the right knee joint, as illustrated in Figures 1, 2, and 3. Both showed the condition on admission. Careful examination appeared to show that flexion deformity was the result of the position that had been maintained for some 5 or more years rather than a contraction of the skin as there was no scar evident over the popliteal region.

September 9, 1933. Under ether anesthesia, Kirschner wire was passed through the os calcis and skeletal traction as illustrated. No rest left necessary to apply traction in the upper tibia as while under anesthesia the os calcis traction there was 40 degree correction of the deformity.

September 27, 1933. Flexion contracture was completely corrected and the traction maintained patient can actively flex knee to right angle. 10th case. A Thiersch graft was then applied over the granulating area previously treated with ultra violet light and Dakin solution. The graft was successful and the ulcer healed in 10 days time.

August, 1934. Since the above procedure, the patient has had no further complaint, either as regards recurrence of the ulcer or of the deformity contracture. Both completely corrected. Present condition is shown in Figures 3 and 4. Patient has normal range of flexion and extension of both knee joints. She returned to school and full activities.

A static flexion contracture of right knee joint of 5 years duration due to short gastrocnemius and faulty posture was present in a schoolgirl of 17 the result of old severe burns of both lower extremities, persistent ulcer of anterior inferior knee region.

Flexion contracture was corrected following skeletal traction of 1 week applied through os calcis. Ulcer was then grafted and healed in 10 days time.

Follow up 11 months, showed normal motion in knee joint, ulcer still healed, usual activities indulged.

Case 9. Mrs. Catherine M., aged 5 years, borned 1928. Diagnosis: bilateral anterior knee flexion deformity, 5 years duration.

February 7, 1934. Patient was admitted to clinic with complaint that for the past 5 years she has experienced increasing difficulty in sitting because of pain and inability to straighten the knee joints. For the same reason the patient also stated that in the preceding 3 years she has walked progressively less. During the past 3 months discomfort in the knees has been so marked when she attempted to stand and sit that she now resorts to her help. She has had no previous treatment; the knees but has had various medications and tonics such as her mother.

Examination of the knees and hip joints showed flexion deformity in both legs of 5 to 20 degrees in the left knee joint, flexion deformity of 30 degrees on the right. 5 degrees. Figure 1 is photograph of the patient showing the position assumed when standing before treatment was instituted.

February 23, 1934. Under ether anesthesia the hip flexion deformity was easily corrected by gentle manipulation. By progressive repeated gentle manipulation, the flexion deformity of the right knee was completely corrected and long leg plaster was applied. On the left side the maximum amount of extension obtained was 30 degrees. 10th patient fully relaxed, 30 degrees less than her normal range of extension. A Kirschner wire was therefore passed through the os calcis and the patient put up in traction.

February 28, 1934. Complete correction of flexion deformity in both legs was obtained. Figure 2 shows the complete correction, the right leg in plaster and the left leg in skeletal traction through os calcis.

March 4, 1934. Patient discharged from the hospital carrying caliper brace on the left leg, walking well, with full extension of both knee joints. Knee flexion normal.

August, 1934. Patient returned for check up examination. Figures 3, 4, and 5, photographs taken at this time, both show maintenance of full correction of the flexion deformity in both lower extremities and also exhibit normal range of flexion in the left knee which is likewise present in the right. All the reaction and swelling about these joints has disappeared.

Bilateral arthritic knee flexion contracture of 2 years' duration in a housewife, aged 51, was corrected by manipulation and by skeletal traction in 1 week

Follow up, 6 months, showed maintenance of correction, with normal motion of both knee and hip joints

#### BIBLIOGRAPHY

- 1 FITCHET S M "Flexion deformity" of the hip and the lateral intramuscular septum New England J Med, 1933, 209 74
- 2 FOERSTER, G Surgical treatment of neurogenic contractures Surg, Gynec & Obst, 1931, 52 366
- 3 HAGGART, G E Avertin anesthesia in bone and joint surgery Am J Surg, 1933, 22 509
- 4 KULOWSKI, J Flexion contracture of the knee J Bone & Joint Surg, 1932, 14 618
- 5 SILVER, D The rôle of the capsule in joint contracture with special reference to subperiosteal separation J Bone & Joint Surg 1927 8 96
- 6 STEINDLER, A The mechanics of muscular contractions in wrist and fingers J Bone & Joint Surg, 1932, 14 1
- 7 YOUNT T C The rôle of the tensor fasciae femoris in certain deformities of the lower extremities J Bone & Joint Surg, 1926, 8 171
- 8 WILSON, P D Posterior capsuloplasty in certain flexion contractures of the knee J Bone & Joint Surg, 1929, 11 40

## GRANULOSA CELL AND BRENNER TUMORS OF THE OVARY

REPORT OF A CASE WITH A REVIEW OF THOSE CASES ALREADY RECORDED

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THE profound influence exerted by the normal follicular elements of the ovary on the proper functioning of the organs of reproduction has been established by numerous workers during the past few years. It has been discovered also that some neoplasms of the ovary are capable of assuming a phase of "physiologic" activity.

It remained for Robert Meyer (48-53) and Neumann (56-60) among others to emphasize that in special types of ovarian neoplasms, the tumor cells retain their secretory function peculiar to the type of cell which they morphologically resemble. Recent investigators (Meyer, Abraham, Neumann) have noted that enlargement of the uterus, hyperplasia of the endometrium, and menstrual irregularities may be associated at times with new growths of this character.

In the present paper the available literature pertaining to the two most common forms of epithelial neoplasms of the ovary—described under many different names—which structurally imitate normal ovarian architecture has been reviewed. These are (1) the granulosa cell neoplasm and (2) the oophoroma folliculare or Brenner tumor.

The granulosa cell tumor especially is composed of tissue morphologically and functionally—if the term function may be applied to a neoplasm—similar to the ovarian parenchyma. Widespread controversy has arisen concerning these singular epithelial growths, chiefly because of the various designations applied to them and, also, because of the varied histological features one may find in different areas of the same tumor.

In this paper all recorded cases of epithelial tumors of the ovary in which the follicular architecture was outstanding have been collected and analyzed. We have made every effort to separate the folliculoma ovarii (granulosa cell tumor) from the Brenner tumor (oophoroma fibro-epithelioma mucinosum benignum).

In certain instances this investigation was beset with considerable difficulty and in others proved well-nigh impossible. This difficulty arose because several authors applied the names folliculoma and oophoroma to the same type of tumor or employed either term indiscriminately. For instance the tumors described by Loennberg, Voigt, Gottschalk, and Ingwers as folliculomata are, we believe, growths of the Brenner type.

In Tables I and II there are portrayed summarizations of the cases of these two varieties of tumor as described in the literature. Tumors identified as granulosa cell growths are listed in Table I and those falling in the Brenner category in Table II.

More or less complete data, both clinical and pathological, of 160 granulosa cell tumors, and 66 Brenner tumors, have been reviewed, making a total of 226 cases.

Several authors reported their personal cases of granulosa cell neoplasms in groups or series. For instance, Robert Meyer records 13 cases. Kermanner 50 cases, including one associated with ovarian tuberculosis. Novak recently registered 23 cases. Adding the foregoing 85 cases to the number previously mentioned, 226, brings the grand aggregate—forming the basis of this paper—to 312.

The granulosa cell neoplasm (folliculoma ovarii carcinoma ovarii folliculoides) refers to that variety of neoplasm of the ovary consisting of collections of large cells resembling the normal granulosa cells of the graafian follicle.

In the typical type of the tumor the cells are characteristically arranged in round or oval masses associated in certain specimens with cysts. In some instances the cells are architecturally arranged in the form of cords or trabeculae. Occasionally the cellular formation may appear in solid masses containing areas of hyaline degeneration, which impart to the growths the appearance of cysts. In still other types the cells may be disposed in a variety of ways.

In certain sections of the tumor the cells may assume a follicle-like structure, while in other areas the disposition may be in the form of cords or strands.

According to Meyer the Brenner tumor both macroscopically and microscopically differs materially from the granulosa cell neoplasm. Genetically it is related to the group of serous cystomata, as well as to the adenomatous, papillomatous, and partial fibromatous cysts.

This growth displays a special tendency to develop cavities of varying size. These usually contain either colloid or mucoid material or both.

The growth may occur as an individualistic small solid mass composed of cylindrical cells

with or without cystic alteration. It may, moreover, arise in conjunction with large pseudomucinous epithelial ovarian cysts.

#### HISTORICAL

In 1890, Acconci observed a papillary growth of the ovary in which he found ovum-like bodies and in which the parenchyma assumed a follicle-like formation. Emanuel, about the same time, encountered similar findings in a bilateral ovarian carcinoma and he, accordingly, advanced the theory of the possible transformation of follicular cells into carcinomatous cells.

In 1894, there appeared articles by Mengershausen and von Kahliden describing unilateral ovarian neoplasms which showed characteristic carcinomatous formation with alveolar structure. The former author applied the term adenoma of the follicle to the growth, believing that the neoplasm arose from the follicular epithelium.

Later authors described ovarian tumors displaying this peculiar characteristic and applied various terms to them, such as folliculoma ovarii malignum (Gottschalk), carcinoma folliculoides (Meyer, Blau), cylindroma (Glockner), granulosa cell tumor (Werdt), and fibroma ovarii adenocysticum (Frankl).

Brenner, in 1907, described three tumors found in elderly women. These consisted of a cellular stroma, in which were scattered spherical and oval areas of epithelial nests. The epithelium of these nests consisted for the most part of large polygonal cells with nuclei rich in chromatin. To this tumor Brenner applied the term *oophoroma folliculare*.

Although in some respects similar to the folliculoma (granulosa cell tumor), it is accompanied with a symptomatology somewhat divergent and it probably has a different histogenesis.

Plaut recently suggested for the Brenner tumor a name which describes the essential features of the neoplasm—*fibroepithelioma mucinosum benignum*.

#### HISTOGENESIS

With regard to the histogenesis of the granulosa cell neoplasm, Meyer is inclined to believe that the cells of the tumor originate in embryonal parenchyma rests (*Granulosa-ballen*). It is the conviction of this observer that the origin of a neoplasm from adult granulosa cells is extremely unlikely. He bases his belief on the assumption that the development of these cells is dependent entirely upon the life of the ovum. He offers, as additional support of his hypothesis, the histological character of the tumor cells, the tendency to follicle-like formation, and finally the effect of the "functioning" neoplasm on the endometrium.



FIG. 1. Photomicrograph of granulosa cell tumor occurring in a child 11½ years of age. Reported by Dr. Robert Meyer.

Evidence adduced from the microscopical appearance of very early tumors of the granulosa cell type, as reported by Te Linde and Geist, together with the findings of embryonal cell rests in the ovaries of the newborn, would seem to indicate that the probable origin is in the embryonic rests of the ovarian parenchyma in the medullary portion of the ovary.

The epithelial construction or content of the Brenner tumor, on the other hand, does not arise from the ovarian parenchyma, but has its derivation, according to Meyer, from special cells which have no relation to the normal tissue structure of the ovary.

It is not unlikely that the Brenner tumors, as well as the ordinary pseudomucinous cystomata, develop from Walthard's rests of cells in the original germinal layer of epithelium.

#### PATHOLOGY

Grossly the granulosa cell tumor may vary in size from a mere microscopic nodule to a growth from 15 to 20 centimeters or more in diameter. In outline the tumor is usually spherical or ovoid. Sometimes the neoplasm is irregular in contour. In appearance and consistence it resembles a solid growth. In color it is usually pinkish white, but not the "dead" or "pearly white hue" which one finds in a typical adenocystoma.

The tumor is invariably encased in a rather thick, dense, fibrous capsule. As a rule, it is freely movable and not adherent to the circumjacent structures. A large tumor is almost

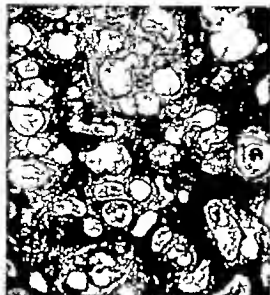


Fig. 2a. Brenner tumor. This photomicrograph presents characteristic picture at low power. Irregular, anastomosing, epithelial masses varying in shape. They are partly hollow. They contain masses. Narrow hyaline bands surround the epithelium. They are small cysts (Papan).

invariably associated with a varying degree of ascites. On section it is found generally partially cystic and partially solid. The incised surface is of a yellowish color and shows more or less necrotic alteration.

Histologically the neoplasm may be placed in one of three oncologic groups, according to the predominating type and arrangement of the epithelial cells. Type 1—ovarian carcinoma with folliculoid structure (*carcinoma folliculoides ovarii*). Type 2—ovarian carcinoma with preponderance of cylindroid structure (*carcinoma cylindroides ovarii*). Type 3—ovarian carcinoma with mixture of folliculoid and cylindroid structure (*carcinoma folliculoides et cylindroides ovarii*) (Fig. 2).

The follicle-like bodies are composed of round cells of the granulosa type in which, in some instances, there are found inclusions resembling ovaries. The presence of the latter was erroneously regarded by Emanuel as actual ovarian structures.

Meyer has looked upon these areas of inclusion as collections of colloid material.

As regards the Brenner tumor, this is found in two varieties: (1) the solid form and (2) in association with pseudomucinous cystomata (Figs. 2a and 2b). The solid growth may occur with or without cysts of varying size. These cysts may

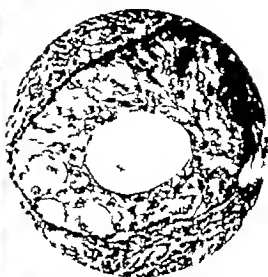


Fig. 2b. Brenner tumor. Partly hollowed out, section containing epithelial mass. The outermost cells are conspicuous by their small, dark nuclei (Papan).

be lined with cylindrical epithelium which secretes a mucoid material. The other type appears in the form of nodules or neoplastic masses in the wall of pseudomucinous cysts. Brenner tumors arising in ovarian cysts have been described by Lahm, Frankl, Fleischmann, and others.

The growth itself, however, may vary in size from a minute nodule to a tumor comparable in size to a child's head. As a rule the development of the neoplasm is rather slow and rarely does it attain large proportions. Ordinarily it may be compared in size to a cherry or small orange. The neoplasm belongs to the carcinomas. Because the clinical course of the growth is relatively benign, many authors believe that the tumor should be placed not in the malignant but in the benign category.

#### CLINICAL FEATURES

The granulosa cell tumor usually involves one ovary although several cases of bilateral involvement have been observed. Ordinarily the neoplasm does not show a tendency to metastasize.

As already mentioned, in size the neoplasm varies from a microscopic particle to a growth as large as a human head. With reference to age, it has been found that the tumors may arise at any period, though they are found most frequently during the menopausal years or shortly thereafter.

The growth as a rule does not excite outspoken symptoms until it attains the size of an orange or larger. Because the cells forming the histological



Fig. 3 Seven year old child prior to removal of a huge granulosa cell tumor of the ovary. Note the precocious development of breasts and heavy growth of pubic hair.



Fig. 4 Roentgenograph of knee joint of child aged 7, with granulosa cell tumor of the ovary, showing 'ripening' of the epiphyses.

background of the neoplasm elaborate the follicular hormone (estron, folliculin), a feminizing effect is produced. This is manifested chiefly in the uterus and is characterized by vascularization, engorgement and hyperplastic alteration of the endometrium. Sometimes the latter becomes so decided as to assume a polypoid phase. Occasionally, the mammary glands participate also in the hypertrophic or hyperplastic process.

The structural and hence the functional changes enumerated herewith arise not only in the sexually active individual but they also occur during the postmenopausal period, or in other words after ovarian function has entirely ceased. Moreover similar changes may occur in the other extreme of life for precocious sexual development in children is a common sequel of the endocrinologic function assumed by the cells marking the morphologic histology of the tumor.

Clinically, granulosa cell tumors are relatively benign, and only rarely do they break through the capsule, recur, or metastasize.

In Habbe's 33 cases, there were only 4 recurrences. In 1 case recurrence took place in the abdominal wall 12 years after extirpation of the tumor. On histologic examination the typical

granulosa tissue structure was found. Roentgen therapy caused regression but death resulted in 1 year, from recurrence.

It is of absorbing interest to note that several specimens of the granulosa cell tumor studied were it is reported associated with myomatous changes in the uterine body. It is therefore, regarded as possible that the hormonal influence of the new growth may be etiologically related to the formation of fibroid tumors just as it is to hyperplastic alteration of the endometrium.

In support of the foregoing assumption, evidence more or less convincing has been set forth by numerous investigators both here and in Europe among whom may be mentioned Novak, Meyer, Schroeder, Fluhmann, Graves and Mazer.

It is generally believed that continuous stimulation by the follicular hormone in the absence of corpus luteum restraint is a common cause of endometrial hyperplasia together with menorrhagia. The excessive production of this hormone by the actively secreting cells of a granulosa cell tumor leads to hyperplasia of the endometrium and subsequent uterine hemorrhage.

A recent study by Witherspoon of 150 cases of uterine myomas, associated with the development



Fig. 5. Photograph of the bilateral granulosa cell tumors (recurrent) removed from a child with precocious sexual development.

of follicular cysts of the ovary combined with excessive estrin secretion, suggests the development of fibromyomatous changes in the myometrium, due it was believed, to prolonged hormonal stimulation.

#### AGE

Of the 150 cases of granulosa cell tumor collected from the literature in which the age of the patient was mentioned it was found that 8 occurred in children under the age of 10 years. Seven were observed in patients aged 1 to 19 years. In 65 (43 per cent) the tumors arose between the twentieth and forty-ninth year. Seventy or 47 per cent of the growths developed in women aged 50 years or more or beyond the menopausal period (Table III).

In a study of the age period with regard to the Brenner tumor it was found that the growth most commonly developed after the menopause. In 62 cases of this type recorded in the literature and in which the age was registered 36 (58 per cent) arose in women well past the menopausal years. No case was recorded as arising in individuals under the age of 20 years.

In Table IV there are tabulated the chief symptoms manifested by 117 patients with tumors of the granulosa cell type. Uterine bleeding (menorrhagia, metrorrhagia) was the most frequent complaint. More than 60 per cent of the 117 patients suffered from uterine hemorrhage of some sort. Eleven patients complained of alternating periods of amenorrhea and menorrhagia. Five had a total absence of the menstrual period. Of the 6

patients showing hypertrophic changes of the breasts, 8 were children who were under the age of puberty. In case (Bingel) the patient became masculinized. It is questionable whether the tumor in this patient was a growth of the true granulosa cell variety.

In Table V the symptoms arising in 55 patients suffering with tumors of the Brenner type are recorded. This growth does not seem to be associated with conspicuous symptoms. In 5 patients there were no local symptoms to attract attention. Not infrequently the tumor was discovered by accident for instance during autopsy or at operation for other conditions. In 8 patients (35 per cent) some form of uterine hemorrhage was experienced. Otherwise no symptom directing attention to the neoplasm was observed, or at least none was recorded.

#### THE GRANULOSA CELL TUMOR AND PRECOCITY

The development of a tumor in the ovary of the granulosa cell form in infants and in young children—because of its elaboration of estrin and stimulation thereby of the reproductive organs—may result often in precocious sexual development (*pubertas praecox*).

In Table VI the clinical records of 8 cases of sexual precocity provoked by granulosa cell tumors of the ovary including our personal case are outlined.

It is likely that re-examination of ovarian neoplasms heretofore encountered in patients with precocious sexual development would disclose a large percentage of granulosa cell neoplasms.



Fig 6 Section of granulosa cell tumor removed from 7 year old child. Low power

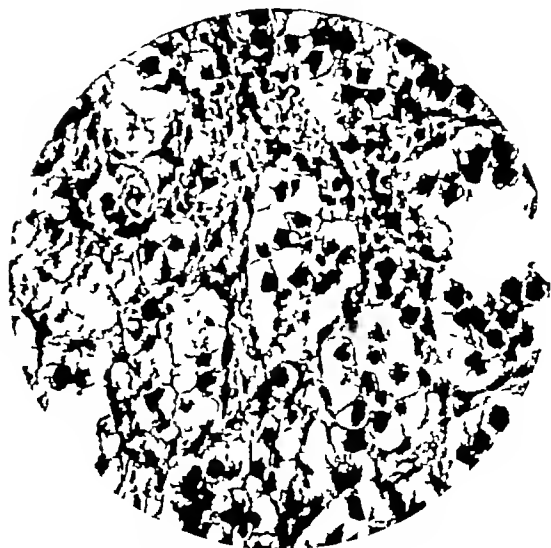


Fig 7 Granulosa cell tumor of the ovary Authors' case High power

#### CASE HISTORY

The patient, I C, aged 7 years, was admitted to the Jefferson Medical College Hospital on June 2, 1931 (Fig 3)

The parents of the child seemed normal in every way. She was the first baby, and the pregnancy ran a normal course of 280 days. The delivery was not seriously complicated, although it was somewhat prolonged and was terminated by forceps. Both the physical and mental development of the child was somewhat tardy. Because of rickets, she did not walk until nearly 3 years of age.

Four months before admission to the hospital, she had a normal menstrual period, that is, normal as regards duration and quantity of flow. Up to the time of admission the menstrual cycle ran a regular monthly course. Coincident with the advent of menstruation, there was noted conspicuous enlargement of the breasts. At the same time the mother noticed a rather luxurious growth of long, coarse hair over the pubic region and in the axillae. A few weeks prior to admission, there was observed, moreover, considerable distention of the abdomen. This increased quite rapidly shortly before the patient came under observation.

A physical study revealed the child to be subnormal mentally. The head was of the large, square type, with special prominence of the forehead. The breasts in size resembled those of a girl at puberty. The abdomen was markedly distended and was somewhat fluctuant. A large, resistant, globular, though somewhat irregular mass—freely movable—occupied the hypogastric region and extended well above the umbilicus. The distention was not painful, nor was it tender.

An examination of the blood showed a hemoglobin of 80 per cent, a red cell count of 4,150,000, and a leucocyte count of 17,500. There were 432,000 blood platelets and the bleeding time was 4 minutes. The serologic tests—Wassermann and Kahn—were negative. The blood calcium was 9.28 milligrams, the blood phosphorus 4.8 milligrams, and the blood sugar 74 milligrams.

On June 4, two days prior to the removal of the tumor by laparotomy, the estrin pregnancy test was positive. The

Aschheim Zondek test was negative. A roentgenological examination of the abdomen revealed the lower portion to be uniformly dense. This had the appearance of being caused by a soft tissue mass. The colon with its mesentery was displaced upward. The kidneys appeared to be in normal position and of average size. There was no evidence of calculi in the urinary tract, nor could any pathologic vertebral or bone changes of the pelvis be discovered.

The sella turcica seemed to be within normal limits and the clinoids were well formed. There was no sign of intracranial disease. There was, however, pronounced "ripening" or precocious development of the epiphyses in the lower end of the humerus and at the upper end of each radius. The epiphyses in the upper and lower ends of each femur showed signs of maturity, since these had united with the diaphyses of the respective bones. This fusion had taken place extremely early and from 7 to 10 years earlier than under normal conditions.

On June 6, 1931, the patient was operated upon. A midline abdominal incision was made and the tumor exposed. This was found to spring from the left ovary. The neoplasm with the left fallopian tube was removed.

The right ovary was examined and it was in all respects apparently normal.

The recovery of the patient was not eventful and she was discharged on the twenty first postoperative day.

On the seventh day following operation the estrin pregnancy test was performed and it was found negative.

*Pathologic report* (Dr B. L. Crawford) The specimen consists of a somewhat rounded, but slightly flattened, mass which measured 18 by 14 by 8 centimeters. It weighed 1250 grams. The external surface—of a pinkish, yellowish, white hue—was fairly smooth, though somewhat bossed. On one surface a portion of the fallopian tube was attached. No gross signs of ovarian tissue were observed. The neoplasm was definitely encapsulated (Fig 5).

On section the tumor was composed of more or less homogeneous tissue—grayish white in color—which,



TABLE I.—SUMMARY OF GRANULOSA CELL TUMORS OF THE OVARY RECORDED IN THE LITERATURE

No.	Year	Author	Age	Diagnosis	Chief symptoms and associated conditions	Outcome
1	1860	Accorsi	Not given	Follicle formation in ovary	Not stated	Not given
2	1867	Kausand	60	Ovarian tumor with follicular structure	Abdominal pain	Microscopic
3	1861	Morgagni	Not given	Adenocarcinoma follicular ovary	Abdominal tumor	Not given
4	1865	Lublin	Child	Adenoma of granular follicle	Not stated	Not given
5	1866	Schneider	26	Policystoma	Pain, irregular periods	Not given
6	1869	Kocher	26	Follicular adenoma of Graafian follicle	Not stated	Not given
7	1871	Glickman	24	Cystadenoma	Not stated	Dead in 10 days, autopsy
8	1871	Ward	24	Folliculoma	Abdominal pain	Death in 4 months
9	1871	Ward	25	Cystoma ovary with folliculoma	Abdominal pain	Recovery
10	1871	Ward	60	Policystoma	Not stated	Tumor in ovary
11	1871	Ward	25	Ovarian cell tumor	Menorrhagia	Not given
12	1871	Ward	8	Ovarian cell tumor	Abdominal pain, menorrhagia	Not given
13	1871	Ward	8	Ovarian cell tumor	Abdominal pain, menorrhagia	Not given
14	1874	Otto	21	Tumor from antral follicle of ovary	Carries on of opposite ovary	Not given
15	1874	Archer	Not given	Ovarian cell tumor	No definite symptoms in ovary	Dead in 4 months
16	1877	Archer	25	Ovarian cell tumor	Menorrhagia and amenorrhea	Went after 14 years
17	1877	Schneider	45	Ovarian cell tumor	Not stated	Not given
18	1878	Bertram	20	Follicular carcinoma	Not stated symptoms	Not given
19	1878	Kocher	22	Ovarian carcinoma	Menorrhagia enlarged uterus	Dead, microscopic examination
20	1878	Linder-Kocher	26	Adenoma of the corpus uterini	Menorrhagia	Recovery
21	1878	Nussbaum	30	Carcinoma follicularis	Not stated	Dead in 4 months
22	1878	Nussbaum	24	Carcinoma with follicular structure	Not stated	Went in 10 years
23	1878	Nussbaum	26	Ovarian cell tumor	Irregular periods	Went in 10 years
24	1878	Nussbaum	25	Carcinoma follicularis	Not stated	Went in 10 years
25	1878	Nussbaum	26	Mucillary carcinoma of follicle type	Not stated	Went in 10 years
26	1878	Nussbaum	25	Adenocarcinoma of follicle type	Not stated	Dead, days postoperative
27	1878	Ward	27	Ovarian cell tumor (adenoma)	Menorrhagia symptoms	Went after 10 years
28	1878	Ward	25	Follicular ovary adenoma	Not stated	Went in 10 years
29	1878	Ward	25	Ovarian cell tumor and fibroma	Not stated	Not given
30	1878	Ward	25	Fibroma and adenoma	Not stated	Not given
31	1878	Ward	25	Ovarian cell tumor (adenoma)	Not stated	Not given
32	1878	Ward	25	Carcinoma follicularis	Not stated	Not given
33	1878	Ward	25	Carcinoma of the ovary	Abdominal pain and bleeding	Recovery
34	1878	Ward	25	Carcinoma of the ovary	Not stated	Not given
35	1878	Ward	25	Carcinoma of the ovary	Extreme bleeding, right ovarian	Recovery
36	1878	Ward	25	Follicular carcinoma	Not stated	Not given
37	1878	Ward	25	Ovarian cell tumor	Abdominal pain, vaginal bleeding	Went after 10 years
38	1878	Ward	25	Ovarian cell tumor	No definite bleeding, 10 years after	Not given
39	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
40	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
41	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
42	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
43	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
44	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
45	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
46	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
47	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
48	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
49	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
50	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
51	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
52	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
53	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
54	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
55	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
56	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
57	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
58	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
59	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
60	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
61	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
62	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
63	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
64	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
65	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
66	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
67	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
68	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
69	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
70	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
71	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
72	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
73	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
74	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
75	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
76	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
77	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
78	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
79	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
80	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
81	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
82	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
83	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
84	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
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86	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
87	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
88	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
89	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
90	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
91	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
92	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
93	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
94	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
95	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
96	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
97	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
98	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
99	1878	Ward	25	Ovarian cell tumor	Not stated	Not given
100	1878	Ward	25	Ovarian cell tumor	Not stated	Not given



TABLE I—SUMMARY OF GRANULOSA CELL TUMORS OF THE OVARY RECORDED IN THE LITERATURE—Continued

No.	Year	Author	Age	Diagnosis	Chief symptoms and associated conditions	Outcome
83	91	Habbe	41	Granulosa cell tumor (antral)	Uterine bleeding	Died postoperative peritonitis
84	1911	Habbe		Granulosa cell tumor (antral)	Irregular and profuse menses	Went at years
85	1911	Habbe	43	Granulosa cell tumor (antral)	Amenorrhea and bleeding	Went at years
86	1911	Habbe	37	Granulosa cell tumor (antral)	Irregular menses, amenorrhea	Went at years
87	1911	Habbe	51	Granulosa cell tumor (antral)	Irregular menses	Went at years
88	1911	Habbe	30	Granulosa cell tumor (antral)	Bleeding, 2 weeks	Went at years
89	1911	Nichols	1	Granulosa cell tumor (antral)	Postmenopausal bleeding	Went at years
90	1911	Nichols	39	Granulosa cell tumor (antral)	Uterine bleeding, 14 years	Not given
91	1911	Nichols	Not given	Granulosa cell tumor (antral)	Not stated	Not given
92	1911	Nichols	43	Granulosa cell tumor (antral)	Postmenopausal bleeding	Not given
93	1911	Nichols	46	Granulosa cell tumor (antral)	Abdominal tumor (recurrent years)	Recovery
94	1911	Nichols		Granulosa cell tumor (antral)	Uterine bleeding	Went at years
95	19	Nichols	23	Granulosa cell tumor (antral)	Uterine bleeding	Not given
96	1911	Nichols	40	Granulosa cell tumor (antral)	Recurrent tumor in vagina	Not given
97	1901	Nichols	48	Granulosa cell tumor (antral)	Uterine bleeding	Not given
98	1911	Nichols (Kahn note)	1	Granulosa cell tumor (antral)	Same pregnancy	Went at years
99	1901	Feld		Granulosa cell tumor	Same pregnancy	Recovery
100	1911	Weyer	14	Granulosa cell tumor	Same pregnancy	Went at years
101	1911	Mendelsohn	Unknown	Follicular cystitis	Not stated	Not stated
102	1911	Mendelsohn	Unknown	Follicular cystitis	Not stated	Not stated
103	1901	Dowrick	37	Granulosa cell tumor	Uterine bleeding years	Went at years
104	1901	Lippert	60	Granulosa cell tumor (cytological)	Postmenopausal bleeding	Went at years
105	1911	Lippert	48	Granulosa cell tumor (cytological)	Not stated	Went at years
106	1901	Lippert	54	Granulosa cell tumor (cytological)	Uterine bleeding	Not given
107	1911	Lippert	34	Granulosa cell tumor (antral)	Uterine bleeding, years	Went at years
108	1911	Lippert	34	Granulosa cell tumor (antral)	Amenorrhea, bleeding	Went at years
109	1911	Lippert	37	Granulosa cell tumor (antral)	Amenorrhea, bleeding	Went at years
110	1911	Lippert	30	Granulosa cell tumor (cytological)	Postmenopausal bleeding	Went at years
111	1911	Belknap	41	Granulosa cell tumor (antral)	Abdominal swelling, metastasis to bone	Died, 10 days
112	1911	Farrar	44	Granulosa cell tumor (antral)	Uterine bleeding	Went at years
113	1901	Farrar	36	Granulosa cell tumor (follicular)	Uterine bleeding, years	Went at years
114	1911	Farrar	30	Granulosa cell tumor (antral)	Postmenopausal bleeding	Recovery
115	1911	Farrar	60	Granulosa cell tumor (cytological)	Uterine bleeding, 6 months	Died in the postoperative
116	1911	Farrar	Not given	Granulosa cell tumor	Uterine bleeding, menses	Went at years
117	1911	Farrar	71	Granulosa cell tumor (cytological)	Abdominal tumor, uterine bleeding	Recovery
118	1911	Farrar	60	Atypical granulosa tumor (antral)	Abdominal tumor, uterine bleeding	Died during operation
119	1911	Farrar	45	Recurrent granulosa cell tumor	Abdominal tumor, amenorrhea	Went at years
120	1911	Welford	30	Granulosa cell tumor	Irregular menses	Not given
121	1911	Welford	22	Granulosa cell tumor	Uterine bleeding	Not given
122	1911	Welford	14	Granulosa cell tumor	Menstrual disturbances, bleeding	Recovery
123	1911	Welford	41	Granulosa cell tumor	Abdominal pain	Recovery

TABLE I—SUMMARY OF GRANULOSA CELL TUMORS OF THE OVARY RECORDED IN THE LITERATURE—Continued

No	Year	Author	Age	Diagnosis	Chief symptoms and associated condition	Outcome
124	1932	Heidler	37	Granulosa cell tumor	Amenorrhea	Recovery
125	1933	Neumann	44	Granulosa cell tumor (bilateral)	Abdominal pain metastasis	Died in 1 yr no operation
126	1933	Neumann	45	Granulosa cell tumor (bilateral)	Bleeding peritoneal metastasis	Died in 1½ years
127	1933	Neumann	over 50	Granulosa cell tumor (bilateral)	Abdominal swelling peritoneal metastasis	Died in ½ year
128	1933	Neumann	54	Granulosa cell tumor	Abdominal swelling and pain	Died in 6 months
129	1933	Neumann	46	Granulosa cell tumor	Uterine bleeding	Not given
130	1933	Neumann	61	Granulosa cell tumor	Postmenopausal bleeding	Not given
131	1933	Plate	23	Folliculome lipidique (Lecene)	Uterine bleeding 6 weeks amenorrhea	Recovery
132	1933	Szathmary	44	Granulosa cell tumor bilateral (cylindroid)	Irregular menses abdominal pain	Died in 2 years
133	1933	Szathmary	46	Granulosa cell tumor (folliculoid)	Irregular menses abdominal pain	Died in 6 yrs acute infection
134	1933	Szathmary	56	Granulosa cell tumor (folliculoid)	Irregular bleeding carcinoma of uterus	Recovery
135	1933	Szathmary	51	Granulosa cell tumor	Abdominal tumor	Recovery
136	1933	Szathmary	47	Granulosa cell tumor	Amenorrhea and menorrhagia	Not given
137	1933	Szathmary	45	Granulosa cell tumor (folliculoid)	Amenorrhea and bleeding carcinoma of uterus	Recovery
138	1933	Szathmary	33	Granulosa cell tumor (folliculoid)	Uterine bleeding and amenorrhea	Recovery
139	1933	Szathmary	51	Granulosa cell tumor (cylindroid)	Abdominal tumor ascites	Recovery
140	1933	Szathmary	64	Granulosa cell tumor (folliculoid)	Abdominal tumor 16 yrs. diabetes	Died after operation
141	1933	Brewer	63	Hyperplasia of granulosa cells	Menorrhagia	Not given
142	1933	Brewer	50	Hyperplasia of granulosa cells	Irregular bleeding	Not given
143	1933	Brewer	34	Hyperplasia of granulosa cells	Menorrhagia	Recovery
144	1933	Wolfe	27	Granulosa cell tumor	Uterine bleeding abdominal enlargement	Well at 6 months
145	1933	Wolfe	48	Granulosa cell tumor	Abdominal tumor	Well at 5 years
146	1933	Daily	38	Granulosa cell tumor	Menopausal 6 years no bleeding	Recovery
147	1933	Daily	27	Granulosa cell tumor	Amenorrhea 16 months	Not given
148	1933	Schulze	54	Granulosa cell tumor	Uterine bleeding 7 years	Recovery
149	1933	Schulze	54	Granulosa cell tumor	Uterine bleeding 2 months	Well at 11 months
150	1933	Schulze	47	Granulosa cell tumor	Uterine bleeding abdominal pain	Well at 1 year
151	1933	Schulze	27	Granulosa cell tumor	Menorrhagia	Well at 15 years
152	1933	Schulze	Not given	Granulosa cell tumor	Not stated	Died in 4 years
153	1933	Schulze	Not given	Granulosa cell tumor	Not stated	Not given
154	1933	Schulze	51	Granulosa cell tumor	Irregular bleeding	Well at 2 months
155	1933	Lellbach	60	Granulosa cell tumor	Irregular bleeding	Recovery
156	1933	Novak	4	Granulosa cell tumor	Sexual precocity	Well at 2 years
157	1933	Novak	5	Granulosa cell tumor	Sexual precocity	Unknown
158	1933	Novak	6	Granulosa cell tumor	Sexual precocity	Well at 1 year
159	1934	Bland	8	Granulosa cell tumor (recurrent)	Sexual precocity	Well at 1 year
160	1934	Kearbey	53	Granulosa cell tumor	Profuse menstrual bleeding myoma	Recovery

Granulosa cell tumors reported in groups Meyer—12 Kermauner—50 Novak—23 Total—85

TABLE II.—SUMMARY OF BRENNER TUMORS OF THE OVARY RECORDED IN THE LITERATURE

No.	Year	Author	Age	Diagnosis	Chief symptoms and associated conditions	Outcome
189	1899	Amann	65	Papillary serous tumor	Not stated, carcinoma of cervix	Not given
190	1899	Orlitzman	64	Abundant cystic carcinoma- toma ovary	Abdominal pain, ascites	Went at 4 years
191	1899	Orlitzman	47	Papillary serous carcinoma ovary	Irregular bleeding	Not given
192	1899	Orlitzman	Not given	Adeno-fibrous carcinoma	Not stated	Not given
1	1901	Lauenberg	36	Carcinoma follicularis malignum	Abdominal swelling bilateral	Died in 8 months
2	1904	Guthrie	48	Follicularis ovary malignum	Abdominal swelling, ascites	Went at 2 1/2 years
3	1904	Valer	47	Carcinoma follicularis ovary	Abdominal pain, bilateral, metastases	Died in 6 months
4	1907	Brenner	64	Oophorectomy follicularis	Not stated	Died 8 days, postoperative
5	1907	Brenner	Old woman	Oophorectomy follicularis	Not stated	Fatal at autopsy
6	1907	Brenner	72	Oophorectomy follicularis	Not stated	Fatal at autopsy
7	1907	Ingalls	66	Follicularis ovary	Bilateral abdominal tumor, menorrhagia, ascites	Died after operation
8	1908	Flower	21	Adenoma pseudomucinosum	Not stated, large pseudomucinous cyst	Went at 10 years
9	1904	Liden	51	Brenner tumor	Menorrhagia pseudomucinous cyst	Went at 12 years
10	1904	Flower	41	Cyst with Brenner tumor	Menorrhagia	Went at 4 years
11	1909	Dankwardt	34	Oophorectomy follicularis	Abdominal swelling and pain, tumor mass in other ovary	Recovery
12	1909	de Ligny	23	Brenner tumor	Abdominal swelling pseudomucinous	Went at 2 1/2 years
13	1911	Bulford	64	Oophorectomy	Not stated	Fatal at autopsy
14	1911	Krasnapolch	66	Follicular carcinoma	Bilateral, carcinoma of liver	Fatal at autopsy
15	1911	Krasnapolch	Not given	Follicular carcinoma	Not stated	Not given
16	1911	Mossman	36	Brenner tumor	Not stated	Not given
17	1917	Frankl	44	Fibroma ovary adenocystic (left)	Abdominal swelling, pain, bleeding left ovarian tumor	Not given
18	1917	Frankl	36	Brown cysts and Brenner tumor v	Not stated	Went at 14 years
19	1917	Frankl	64	Fibroma ovary adenocystic (right)	Enlarged abdomen, left breast of cancer	Not given
20	1917	Frankl	39	Fibroma ovary adenocystic	Enlarged abdomen	Not given
21	1917	Frankl	41	Fibroma ovary adenocystic	Menorrhagia, ovarian pain	Not given
22	1917	Frankl	34	Fibroma ovary adenocystic	Enlarged abdomen bleeding	Not given
23	1917	Frankl	48	Fibroma ovary adenocystic	Abdominal pain, menorrhagia, asc	Not given
24	1917	Frankl	70	Fibroma ovary adenocystic	Enlarged abdomen	Not given
25	1917	Frankl	66	Fibroma ovary adenocystic	Bilateral abdominal tumor, menorrhagia	Not given
26	1921	Frankl	48	Fibroma ovary adenocystic	Irregular bleeding enlarged abdomen menorrhagia	Not given
27	1921	Frankl	33	Fibroma ovary adenocystic	Loss of weight	Not given
28	1921	Frankl	69	Fibroma ovary adenocystic	Uterine bleeding	Not given
29	1921	Frankl	23	Fibroma ovary adenocystic	Enlarged abdomen, bilateral tumor	Not given
30	1921	Frankl	66	Fibroma ovary adenocystic	Abdominal pain, urinary symptoms	Not given
31	1921	Frankl	57	Fibroma ovary adenocystic	Backache, urinary symptoms	Not given
32	1921	Frankl	36	Fibroma ovary adenocystic	Abdominal pain	Went at 1 year
33	1921	Frankl	23	Fibroma ovary adenocystic	Enlarged abdomen	Not given
34	1921	Frankl	34	Fibroma ovary adenocystic	Urinary symptoms	Not given

TABLE II.—SUMMARY OF BRENNER TUMORS OF THE OVARY RECORDED IN THE LITERATURE—Continued

No	Year	Author	Age	Diagnosis	Chief symptoms and associated condition	Outcome
39	1927	Neumann	66	Brenner tumor (left)	Not stated right ovarian cyst	Not given
40	1928	Esser	64	Folliculoma	Found at autopsy	Found at autopsy
41	1929	Richter	54 ✓	Fibroma ovarii adenocysticum	Abdominal pain myomata	Recovery
42	1930	Te Linde	63	Oophoroma folliculare	Irregular bleeding	Well at 1 year
43	1932	Meyer	41 ✓	Brenner tumor	Not stated myomata	Not given
44	1932	Meyer	29 ✓	Brenner tumor (solid)	Not stated	Not given
45	1932	Meyer	Not given	Brenner tumor	Not stated	Not given
46	1932	Meyer	44 ✓	Brenner tumor	Not stated	Not given
47	1932	Meyer	51 ✓	Brenner tumor	Menorrhagia pseudomucinous cyst	Recovery
48	1932	Mandelstamm	26 ✓	Brenner tumor	Abdominal pain	Well at 3 years
49	1932	Schiffmann	60	Brenner tumor	Uterine bleeding urinary incontinence	Recovery
50	1932	Schiffmann	61	Brenner tumor	Uterine bleeding	Not given
51	1933	Plaut	54	Fibro-epithelioma mucinosum benignum	Bleeding abdominal swelling pseudomucinous cyst	Well at 4 years
52	1933	Plaut	37	Fibro-epithelioma mucinosum benignum	Amenorrhea abdominal pain left ovarian fibroma	Well at 1 year
53	1933	Plaut	56	Fibro-epithelioma mucinosum benignum	Abdominal swelling myomata	Well at 2½ years
54	1933	Plaut	52	Fibro-epithelioma mucinosum benignum	Abdominal swelling myomata	Recovery
55	1933	Plaut	37	Fibro-epithelioma mucinosum benignum	Amenorrhea, 4 mos. appendiceal peritonitis	Died after operation
56	1933	Plaut	27	Fibro-epithelioma mucinosum benignum	Intermenstrual bleeding	Died in 10 days peritonitis
57	1933	Plaut	20	Fibro-epithelioma mucinosum benignum	Found at autopsy uterine perforation, pregnancy	Found at autopsy
58	1933	Plaut	75	Fibro-epithelioma mucinosum benignum	Abdominal pain	Not given
59	1933	Abraham	31	Brenner tumor	Uterine bleeding abdominal pain myomata	Recovery
60	1933	Abraham	56	Brenner tumor	Uterine bleeding pseudomucinous cyst	Recovery
61	1933	Szathmary	60	Brenner tumor	Abdominal pain and swelling ovarian cyst, myomata	Well at 2 years
62	1933	Szathmary	49	Brenner tumor	Irregular bleeding ovarian cyst	Not given
63	1933	Szathmary	38	Brenner tumor	Abdominal swelling	Well at 12 years
64	1933	Szathmary	70	Brenner tumor	Abdominal pain, large cystoma	Well at 3 years
65	1933	Szathmary	56	Brenner tumor	Abdominal swelling large cystoma	Recovery
66	1934	Matry	70	Brenner tumor	Bilateral abdominal swelling large cystoma	Recovery

though somewhat resistant, was throughout its extent relatively compressible and soft. The tumor mass was divided into distinct nodules, but there appeared to be a fusion of the tissue forming the nodules, as well as the fibrous septa and capsule. Degenerative changes with areas of edema were found throughout the growth.

Microscopic examination of sections taken from various portions of the tumor revealed that it was composed of rather large polyhedral cells. These contained a clear cytoplasm, but the nuclei, though somewhat small, stained rather deeply. In some sections these cells were loosely arranged in a fibrous tissue stroma, while in others

they formed solid clumps or gland-like areas, and in still others the walls of small cysts. These cyst-like areas bore a strong resemblance to the so called follicular cysts.

Even though numerous sections were taken from all parts of the growth, the cells were found fairly uniform in all. The arrangement also was similar, the only variation was the presence in certain areas of small acini and cysts. No type of epithelium or other structure to suggest a teratomatous mass was observed. The fibrous tissue stroma of the growth was found rather abundant and in certain portions appeared as distinct trabeculae. The stroma was mostly continuous with the fibrous capsule.

TABLE III.—CLASSIFICATION OF PATIENTS ACCORDING TO AGE

Age in years	Grunular cell tumor	Brenner tumor
Under 10	6	
10 to 19	7	
20 to 29		3
30 to 39	3	9
40 to 49	20	
50 to 59	4	16
60 and over	29	20
Not given		4
Total	60	66

TABLE IV.—ANALYSIS OF SYMPTOMS IN 169 PATIENTS

Chief symptoms	Grunular cell tumor—177 patients	Brenner tumor—71 patients
Uterine bleeding (menorrhagia, irregular bleeding, etc.)	70	9
Abdominal tumor	16	
Abdominal pain	3	14
Anaemia	5	2
Urinary symptoms		4
Enlarged breasts		
Sexual precocity	8	
Acne		4
Hypertrophies		
Accidental finding		
Loss of weight		
Mastectomy		
Resectant tumor of vagina		

The cells in general were quite similar in outline. Only occasionally was irregularity noted. The size, together with the contour, was well maintained. Mitoses was not outstanding. So, all in all, there were no signs histologically to indicate high degree of malignancy. From the predominant type of cell, together with the tendency to the formation of acini and cysts, the tumor was looked upon as a member of the granular cell group and accordingly the diagnosis of granular cell tumor of the ovary was recorded.

Following the operation (June 6 '33) the patient did not menstruate for 8 months, or until January '33. At this time the menstrual flow appeared rather unexpectedly and it continued normally for days. At this time some pain was experienced in the lower portion of the right side of the abdomen and examination disclosed considerable distention.

Menstruation returned regularly every 25 days for period of 3 months, or until the patient was readmitted to the hospital on January 5, '33. At this time there was found a large abdominal mass. This was freely movable, somewhat firm in consistency, but not tender.

On the day following re-examination the estrus precocity test was found definitely positive. The Aschheim-Zondek test was, also, positive. The estrus blood test of Link and Goldberger was, likewise, positive as was, also, the anterior pituitary sex hormone test of the blood. This reaction, however, was not decided, but only weakly positive.

A roentgenologic study disclosed a large mass in the lower right portion of the abdomen, which seemed to displace the hepatic flexure of the colon upward.

TABLE V.—SUMMARY OF CASES OF GRANULOSA CELL TUMORS ASSOCIATED WITH SEXUAL PRECOCITY

No.	Author	Age of child	Outcome
1	Blau (Stearns)	5	Well after 1 year
2	Ball		Recovery
3	Habbe (Rosenfeld)	5	Well after 10 years
4	Mayer	14	Well after 10 years
5	Novak		Well after 1 year
6	Novak	5	Unknown
7	Novak	5	Well after 1 year
8	Wood and Goldstein	7	Well after 6 months
*Bilateral Ovaries			

TABLE VI.—FOLLOW UP IN CASES OF GRANULOSA AND BRENNER TUMORS OF THE OVARY REPORTED IN THE LITERATURE

Outcome	Grunular cell tumor	Brenner tumor
Not mentioned	64	27
Recovery from operation	3	10
Well after 1 year	26	14
Well to years or longer	6	2
Died within 1 year	9	
Died during or shortly after operation	7	4
Died after 4 years		
Found at autopsy		6
Died, metastases (no operation)		
Total	160	66

There was no evidence of metastatic disease in the lungs or the mediastinum. There were, furthermore, no X-ray signs of metastases to the skull, to any of the thoracic or lumbar vertebrae, to the bones of the pelvis, or to the bony structures of the extremities.

On April 10, '35, laparotomy was performed and large neoplasm, similar in all respects, as to size, color, contour and consistency, to the growth removed previously was found involving the right ovary. This together with the corresponding fallopian tube was removed. A subtotal hysterectomy was performed at the same time.

The postoperative recovery of the patient was unexceptional and satisfactory in every way.

On the fourteenth day following operation the Aschheim-Zondek and estrus tests of the urine were negative. Six months after the operation, October '35, there was no recognizable regression of the accessory glands. The pubic hair is still present in abundance. At this time the estrus test of the urine was negative, although the anterior pituitary sex hormone test of the blood was weakly positive (Reaction 1). The estrus blood test was negative.

Pathologic report (Dr. B. L. Crawford). The second specimen presented from I.C. consists of a somewhat irregularly shaped, rounded and flattened, tan mass, which weighs 460 grams. It measures by 8.5 by 6 by 6 centimeters. In general this tumor resembles closely the one previously examined.

The sections of the former growth were restudied and the histologic structure of the two neoplasms was found to be

essentially the same. In the second tumor, however, the tissue seemed to contain more edematous fibrous stroma than was found in the first specimen. The tumor cells were identical with those studied in the first specimen and resembled closely granulosa cells. Sections from the uterus were also examined and these showed an endometrium which was quite mature and in the interval stage.

Diagnosis Granulosa cell carcinoma of the ovary

#### ENDOCRINE ACTIVITY OF GRANULOSA CELL TUMOR

Reference to the internal secretory influence of tumors of the ovary of the granulosa cell type in bringing about marked endometrial hyperplasia has been made, particularly by Meyer, Schroeder, Neumann, Habbe, and others.

Hyperplasia of the endometrium with bleeding as an accompaniment, alternating periods of amenorrhea with menorrhagia, is the result of the action of estrin (female sex hormone) produced by the pathologic granulosa cells. In these circumstances the mechanism of the menorrhagia is precisely the same as occurs in the pituitary deficiencies with persistent follicular cyst formation. The typical endocrine effect is noticed in mature and elderly women, in whom there is brought about enlargement of the uterine body and alteration in the endometrium.

Attention has been directed to these changes by numerous observers, including Aschner, Tietze, Neumann, Meyer, and Klawns.

Occasionally one encounters rather profuse and almost continuous bleeding. Indeed, the hemorrhage may be so severe as to lead to profound grades of anemia. This may be followed at times by varying periods of amenorrhea. In sexually active women, the removal of a granulosa cell neoplasm is usually followed by a regular menstrual function.

By laboratory investigation, Schuschania has demonstrated the relationship of the hormonal influence of the granulosa cell tumor on uterine bleeding.

He records the history of a patient, 67 years of age, who was operated upon for a granulosa cell tumor 9 years following the establishment of the menopause. Before operation a quantitative estimation of the total amount of follicular hormone present in the urine and feces—covering a period of 5 days—disclosed 975 mouse units. Within 10 days following operation, there was an impressive reduction in the hormonal content of the excretion, and 10 weeks following the operation no trace of the hormone could be found.

Prior to the second operation in our patient large quantities of the follicular hormone were present both in the blood and in the urine. The absence of this substance in the blood and in the

urine some months after the operation indicated the complete removal of all granulosa cell tissue. The mildly positive Aschheim-Zondek reaction of the blood serum, however, probably was an expression of compensatory effort of the anterior pituitary gland to counterbalance the lack of ovarian activity.

In the numerous reports of the syndrome of sexual precocity recorded in the literature, the condition is ascribed by most authors to disturbances of either the pituitary body, the ovaries, the adrenals, or the pineal gland.

It is pertinent to point out, at this time, that sexual precocity may be caused by the assumption of endocrine activity of ovarian tumors other than the granulosa cell type. Frank, for example, recently reported 2 cases of precocity due in one patient to a malignant teratoma and in the other to an embryonal alveolar carcinoma.

In view of these observations, it is highly probable that microscopic check-ups of ovarian neoplasms removed from patients exhibiting frank signs of sexual precocity would reveal probably in a large number of instances growths falling in the granulosa cell category.

#### ULTIMATE FATE OF PATIENTS WITH GRANULOSA CELL TUMORS

In Table VI there are listed, as recorded in the literature, the ultimate fate of the patients who suffered with granulosa cell tumors of the ovary, as well as tumors of the ovary of the Brenner type. It will be observed that "follow-up" data were available in 96 cases of the granulosa cell tumor and in 39 cases of the Brenner neoplasm.

Recovery following operative removal of the granulosa cell tumor is recorded in 32 patients. Forty-two patients were reported well for periods varying from 1 to 10 years or more after operation. Twenty patients died at varying periods following operation. Two died of metastasis within 1 year—not operated upon. Four died of metastasis within 1 year of operation. The others died of different causes.

With regard to the Brenner tumor it will be observed that 27 of the patients were known to be well at varying periods following removal of the growth (Table VI). Six patients died within 1 year following operation. Of these 4 died within a few days after operation and 2 died within 6 months. One died of metastasis. The cause of death is not given in the 5 others.

#### SUMMARY

1. The available literature regarding granulosa cell tumor of the ovary (folliculoma ovarii) and



the Brenner tumor (oophoroma folliculare) has been reviewed. The clinical data, including the age of the patients, chief symptoms, diagnosis, pathology and the ultimate outcome of the patients, have been presented in tables.

2. Individual summarizations of 160 cases of the granulosa cell tumor and 60 cases of the Brenner tumor are recorded. These together with 85 cases of granulosa cell tumor reported in groups make a total of 311 cases.

3. Clinically the granulosa cell and Brenner tumors are relatively benign. Only occasionally do they break through the capsule recur or metastasize.

4. The granulosa cell tumor occurs most frequently after the menopause. Seventy or 47 per cent, of the growths herein reported developed in women aged 50 years or more. Likewise, it was noted that the Brenner tumor occurred in 36 or 50 per cent of the cases in women well past the menopausal years. Seven cases of granulosa cell tumor however occurred in children under the age of 10 years.

5. Uterine bleeding (menorrhagia, metrorrhagia) was the most common symptom manifested by patients with the granulosa cell tumor. Sixty per cent of the 337 patients in whom symptoms were described complained of this symptom. The Brenner tumor does not seem to be associated with conspicuous symptoms.

6. Granulosa cell tumors occurring in children are prone to induce precocious sexual development. A personal case of a granulosa cell tumor arising in a child 7 years of age, who underwent marked sexual development, is recorded.

7. Data concerning the final outcome were available in 90 cases of the granulosa cell tumor and in 39 cases of the Brenner tumor. Forty two patients with the granulosa cell tumor were reported well for periods varying from 1 to 10 years after operation, while 20 patients died at varying periods following operation. Four of these patients succumbed from metastases within 1 year after removal of the neoplasm. Twenty-seven patients in whom the Brenner tumor was found were known to be well at varying periods following operation. Six died within 1 year after operation. One patient of this group died from metastases.

Since the completion of this article 3 other cases of granulosa cell tumors in children have been described in the literature. E. A. Alfaro (Arch. Gynecol. 1940, 57, 244) reported cases in children 4 and 6 years of age, and H. O. Krumm, in a child 5 1/2 years old. All children exhibited sexual precocity (Arch. Gynecol. 1944, 55, 196).

#### REFERENCES

ABRAHAM, E. G. Brenner tumor and Endometriosis. *Zentralbl. f. Gynak.* 1934, 57 3-5 70

- Idem. Zur Genese der Brenner Tumoren. *Arch. f. Gynak.* 1934, 54 567-573
- ADAMS, J. A. Ueber Bildung von Drüsen und Follikelähnlichen Gebilden im Senilen Ovar. *Kon. Zentralbl. f. Gynak.* 1899, 41 287-288
- ALCANTARA, H. Ueber einen elementaren Ovarialtumor aus der Gruppe der Follikulome. *Arch. f. Gynak.* 1911, 3 350-362
- BARNES, A. Ueber die von Robert Meyer als "das besondere Fata von Carcinom bei weissen und schwarzen nicht Züchtungs Afrikanern beiderlei Geschlechts" bezeichneten Tumoren. *Arch. f. Gynak.* 1927-1928, 35 415-453
- BRUNEL, A. Verschiedenheit von Polyzystischen und Korkbildung einer "Vermischung" nach Entfernung eines Leichnamstümmels des Ovariums. *Deutsch. med. Wochenschr.* 1924, 50 220-222
- BLAY, A. Folliculoma ovarii. *Arch. f. Gynak.* 1906, 26 200-210
- BRUNSON, F. Das Oophoroma folliculare. *Frischbart. Ztschr. f. Path.* 1908, 50-71
- BURWELL, J. I. and JONES, H. O. Granulosa cell hyperplasia of the ovary. *Am. J. Obst. & Gynec.* 1931, 5 307-313
- D'AMICO, J. Sur folliculome ovariel. *Riv. Ital. d. Gynec.* 1930, 105-110
- DROBNIK, H. Ueber einen Fall von Granulosa cell tumor. *Zentralbl. f. Gynak.* 1931, 56 1033-1039
- FISCHL, R. Ueber maligne Ovarialtumoren mit Bildung von Fruchtblasen. *Ztschr. f. Geburtsh. Gynak.* 1902, 27 69-75
- FISCHL, R. Ueber das Follikulom. *Oophoroma ovarii. Monatsschr. f. Geburtsh. Gynak.* 1904, 79 440-445
- FAUPEL, E. Ueber Granulosaaltumoren. *Zentralbl. f. Gynak.* 1912, 36 1085-1100
- FLEISCHMANN, C. Adenofibroma cysticum papillare ovarii. *Zentralbl. f. Gynak.* 1914, 40 417-424
- FLEISCHMANN, C. Clinical and pathological report on three unusual ovarian tumours. *J. Obst. & Gynec. Brit. Emp.* 1925, 30 703-603
- FRANK, R. T. Precocious sexual development in children due to malignant ovarian tumors. *Am. J. Dis. Child.* 1932, 43 947-948
- FRANZ, O. Zur Pathologie und Klinik des Fibroms ovarii endocysticum. *Arch. f. Gynak.* 1917, 3 5 335
- Idem. Scirrhus ovarii bei Granulosaaltumor. *Zentralbl. f. Gynak.* 1914, 35
- GERTZ, S. H. A contribution to the histogenesis of ovarian tumors. *Am. J. Obst. & Gynec.* 1921, 5 5-240
- GILBERT, A. Beitrage zur Kenntnis der soliden Ovarialtumoren. *Arch. f. Gynak.* 1905, 25 49-64
- GOTTSCHE, S. Ueber das Follikulom malignum ovarii. *Berl. klin. Wochenschr.* 1903, 39 607-610
- HAFNER, K. Beitrag zur Frage der Granulosaaltumoren. *Zentralbl. f. Gynak.* 1931, 55 1083-1103
- H. HART, A. COHEN, L. and MORRISON, M. La folliculose de l'ovaire. *Bull. de l'Ass. franc. p. l'Etude du cancer.* 1929, 6 748-607
- HEDDER, quoted by KATZMEYER
- HÖRNER, H. Carcinoma ovarii im Fruchtblase. *Zentralbl. f. Gynak.* 1907, 5 556-557
- INVER, A. Caseistica und kritische Beitrage zum sogenannten Folliculoma ovarii. *Arch. f. Gynak.* 1907, 82 343-363
- KERCKHOF, F. Ueber Granulosaaltumoren der Ovarien, insbesondere bei älteren Frauen mit gleichzeitiger

- Schleimhauthypertrophie des Uterus Zentralbl. f. Gynaek., 1926, 50 89-98.
- 29 KAHLDEN, C. Ueber eine eigenthuemliche Form des Ovarialcarcinoma Zentralbl. f. allg. Path. u. path. Anat., 1895, 6 257-264.
  - 30 KEASBEY, L. E. Personal communication
  - 31 KERMAUNER, F. Die Erkrankungen des Eierstockes. Veit's Handbuch der Gynäkologie. Edited by W. Stoeckel. Vol. 7, p. 331. Munich J. F. Bergmann, 1932.
  - 32 KING, E. S. J. The association of endometriosis with neoplasms of the ovary Surg., Gynec. & Obst., 1929, 49 433-439.
  - 33 KLAFTEN, E. Zur Klinik und Anatomie der Granulosazelltumoren des Eierstockes Monatschr. f. Geburtsh. u. Gynaek., 1930, 86 392-414.
  - 34 KONSCHEGG, T. Onkogenen Riesnwuchs des Uterus Arch. f. path. Anat. u. Physiol., 1923, 242 212-221.
  - 35 KRETSCHMAR. Eine seltene klein-cystische boesartige Geschwulst, Folliculoma malignum ovarii Gottschalk's. Zentralbl. f. allg. Path. u. path. Anat., 1901, 12 643-644.
  - 36 KROMPECHER, E. Ueber die Follikulome, "Oophorome" und "Granulosazelltumoren" des Ovariums Ztschr. f. Geburtsh. u. Gynaek., 1924, 88 341-355.
  - 37 LAHM, W. Zur Histogenese der Pseudomucinkystome des Ovariums Beitr. z. Geburtsh. u. Gynaek., 1914, 19 261-274.
  - 38 LASTRA, E. T., ALTHALA, R., and COLLAS, D. Tumor de ovario a celulas de la granulosa Bol. Soc. de obst. y ginec. de Buenos Aires, 1931, 10 109-117.
  - 39 LELLBACH, A. Ueber den Einfluss der Granulosa-zellgeschwuelste auf den Uterus. Zentralbl. f. Gynaek., 1933, 57 725-729.
  - 40 LEIOS, A. De Eine seltene parenchymatogene Eierstocksgeschwulst mit Ei und follikelaehnlichen Gebilden. Inaugural Dissertation, Heidelberg, 1919.
  - 41 LIPPER, E. H., BAKER, A. H., and DEVAUX, D. M. Granulosa-cell tumours of the ovary Proc. Roy. Soc. Med., 1932, 25 1241-1244.
  - 42 LISSOWETZKY, V. Zur Frage der sogenannten Follikulome des Eierstockes. Arch. f. Gynaek., 1930, 142 477-500.
  - 43 LOENBERG, I. Zur Kenntnis des Carcinoma folliculoides ovarii Nord. med. Ark., 1901, 34 1-27.
  - 44 MANDELSTAMM, A. Beitrag zur Kenntnis des Follikulomes des Eierstockes (Blastom vom Typus Brenner) Arch. f. Gynaek., 1932, 148 494-501.
  - 45 MATSNER, E. Seltene Art von Ovarialgeschwuelsten Arch. f. Gynaek., 1923, 119 5603.
  - 46 MAURA, M. J., and SCHMEISSER, H. C. Report of a case of bilateral ovarian tumors of the Brenner type Am. J. Obst. & Gynec., 1934, 27 200-293.
  - 47 MENGERSHAUSEN. Ueber Carcinom des Ovariums mit Ausschluss des Carcinomatoesen Cystoms Inaugural Dissertation, Freiburg, 1894.
  - 48 MEYER, R. Ueber Carcinoma ovarii folliculoides et cylindromatosum. Ztschr. f. Geburtsh. u. Gynaek., 1915, 77 505-524.
  - 49 Idem. The pathology of some special ovarian tumors and their relation to sex characteristics. Am. J. Obst. & Gynec., 1931, 22 697-713.
  - 50 Idem. Ueber Gewebliche Anomalien und ihre Beziehung zu einigen Geschwuelsten der Ovarien. Arch. f. Gynaek., 1931, 145 2-69.
  - 51 Idem. Ueber verschiedene Erscheinungsformen der als Typus Brenner bekannten Eierstocksgeschwulst, ihre Anordnung von den Granulosa-zelltumoren und Zuordnung unter andere Ovarialgeschwuelste Arch. f. Gynaek., 1932, 148 541-596.
  - 52 Idem. Zur Kenntnis seltenerer Ovarialtumoren. Arch. f. Gynaek., 1918, 100 212-246.
  - 53 Idem. Pathologische Hypertrophie der Uterus-schleimhaut im Gefolge von Ovarialtumoren insbesondere in der Menopause. Zentralbl. f. Gynaek., 1925, 49 1662-1667.
  - 54 MOULONGUET-DOLÉRIIS. Lesdiagnostics Anatomocliniques de P. Lecine, Appareil genital de la femme. 1932, 2 301.
  - 55 MUELLERHEIM, R. Ovarialtumoren bei Greisinnen mit Hypertrophie der Mammæ und des uterus und mit uterinen Blutungen Zentralbl. f. Gynaek., 1928, 52 689-693.
  - 56 NEUMANN, H. O. Störungen des menstruellen Zyklus und pathologische Schleimhauthypertrophie bei Granulosazellcarzinomen. Zentralbl. f. Gynaek., 1925, 49 2695-2703.
  - 57 Idem. Beitræge zur Kenntnis seltener Ovarialblastome Arch. f. Gynaek., 1927, 130 742-765.
  - 58 Idem. Granulosa-zellcarcinoma. (Ein Beitrag zur Frage der Keimepithelblastome des Ovariums) Arch. f. path. Anat. u. Physiol., 1925, 258 284.
  - 59 Idem. Carcinoma folliculoides ovarii s. Folliculoma ovarii Arch. f. Gynaek., 1923, 121 69-91.
  - 60 Idem. Granulosa-zelltumoren als Hormonspeicher Endokrinologie, 1933, 12 166-183.
  - 61 NOVAK, E., and LONG, J. H. Ovarian tumors associated with secondary sex changes—granulosa cell carcinoma and arrhenoblastoma J. Am. M. Ass., 1933, 101 1057-1063.
  - 62 NOVAK, E. Granulosa cell ovarian tumors as a cause of precocious puberty, with a report of 3 cases. Am. J. Obst. & Gynec., 1933, 26 505-521.
  - 63 ORTHMAN, E. G. Zur Casuistik einiger seltenerer Ovarial und Tuben Tumoren Monatschr. f. Geburtsh., 1899, 9 771-782.
  - 64 PAHL, J. Granulosa-zell-tumor im Kindesalter Arch. f. Gynaek., 1931, 147 736-750.
  - 65 PRANNENSTIEL, J. Die Erkrankungen des Eierstockes und des Nebeneierstockes Veit's Handbuch der Gynaekologie, 1908, vol. 14.
  - 66 PICARD, E. Un cas de folliculome typique de l'ovaire. Ann. d' anat. path., 1928, 5 647-653.
  - 67 PLATE, W. P. Ueber Granulosa-zelltumoren des Ovariums. Arch. f. Gynaek., 1932, 151 26-43.
  - 68 Idem. Eine seltene Form eines Granulosa-zell-tumors des Ovariums, das sog. "Folliculome lipidique" (Lecené) Arch. f. Gynaek., 1933, 153 318-331.
  - 69 PLAUT, A. Der sogenannte "Tumor ovarii Brenner" (Fibroepithelioma mucinosum benignum ovarii) Acht neue Faelle. Bemerkungen zur Histogenese. Arch. f. Gynaek., 1933, 153 97-126.
  - 70 RICHTER, J. Zur Kenntnis des sog. Fibroma ovarii Adenocysticum. Wien klin. Wchnschr., 1929, 42 440-442.
  - 71 Idem. Ueber die Histogenese der Adenocystome des Ovarium (unter besonderer Berücksichtigung der Walthardschen Zellinseln) Arch. f. Gynaek., 1927, 130 775-878.
  - 72 ROBINSON, M. R. Folliculoid cancer of the ovary. Am. J. Obst. & Gynec., 1923, 5 581-600.
  - 73 RUMBOLD, P. Ueber Granulosa-zelltumoren. Zentralbl. f. Gynaek., 1931, 55 292-298.
  - 74 SCHNEIDER. Beitrag zu den rezidivierenden Blutungen nach Roentgenkastration Zentralbl. f. Gynaek., 1927, 51 1407-1408.



# EDITORIALS

## SURGERY, GYNECOLOGY AND OBSTETRICS

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AUGUST, 1935

### THE PROBLEM OF GASTRIC RESECTION FOR DUODENAL ULCER

MORE patients, perhaps, are developing recurring ulcer after partial gastrectomy and partial duodenectomy for duodenal ulcer than is apparent from a study of the literature. By gastric resection and removal of the duodenal ulcer, the surgeon hopes to accomplish (1) removal of the ulcerating duodenal lesion, (2) removal of areas of gastritis, involving the antrum of the stomach if such areas are present, (3) reduction of gastric acidity to the point of relative achlorhydria, and (4) relief of pylorospasm and provision of a means of increasing the rapidity with which the stomach empties.

Removal of the duodenal ulcer as a part of gastric resection theoretically is valuable, especially if the lesion is of the hemorrhagic type. This would assume greater importance were it not for the fact that a properly performed gastro-enterostomy resulting in a properly functioning gastro-enteric stoma will be followed by healing of whatever inflammatory

lesions are present in the duodenum, and that removal, in the course of gastric resection, of many of the large, infiltrating, perforating duodenal ulcers carries a risk from five to ten times that of gastro-enterostomy. That removal of a hemorrhagic duodenal ulcer is essential is not a proved fact. Studies of the results of various operative procedures for duodenal ulcer have shown that gastro-enterostomy alone will protect the patient against recurrence of hemorrhage in 82 per cent of the cases, and of equal importance is the fact that, should hemorrhage recur after gastro-enterostomy, it is seldom of serious import.

The association of gastritis and duodenal ulcer is strikingly infrequent among patients operated on at the Mayo Clinic, it occurred in less than 10 per cent of a group of patients on whom gastric and duodenal resection was performed in the treatment of duodenal ulcer.<sup>1</sup> The argument that partial gastrectomy removes, with the duodenal ulcer, the areas of gastritis, and that such areas of gastritis are precursors to the formation of duodenal ulcer in the stomach obviously cannot hold in these cases.

Maintaining reduction of the concentration of hydrochloric acid in the gastric secretion by medical or surgical methods, however, would seem to be of primary importance in the treatment of duodenal ulcer. It should be remembered, however, that achlorhydria occurring subsequent to operation on the stomach for duodenal ulcer, whether the operation is

<sup>1</sup>Walters, Waltman and Sebenius. Walter. A comparison of lesions associated with duodenal ulcer in Germany and in the United States. *Minnesota Med.* 1932 15: 570-584.

Walters, Waltman, and Church. G. T. Gastritis a phenomenon of pyloric obstruction and its relation to duodenal ulcer. *Minnesota Med.* 1935 18: 206-212.

gastric and duodenal resection (partial gastrectomy) or posterior gastro-enterostomy in most cases is a matter of relativity acidity is reduced because of dilution and neutralization of the gastric secretions by reflux of intestinal secretions rather than because of actual failure of the remainder of the stomach to secrete hydrochloric acid. Stimulating gastric secretion by injection of histamine in many cases will produce a measurable secretion of hydrochloric acid even after operation has been performed.<sup>1</sup>

It appears that there is less tendency to recurring ulceration after any operation on the stomach and duodenum for duodenal ulcer if relative achlorhydria occurs. If relative achlorhydria followed in all cases in which partial gastrectomy has been performed, the increased risk of such a procedure over gastro-enterostomy might be warranted. That such a state of relative achlorhydria frequently fails to occur as yet is not well known. In one large series of cases in which subtotal gastrectomy had been performed for duodenal ulcer relative achlorhydria was obtained in but 56 per cent of cases.<sup>2</sup>

On the other hand, a marked reduction in acidity usually occurs following a properly performed posterior gastro-enterostomy with a resulting properly functioning stoma, and in some cases relative achlorhydria is obtained. The degree of reduction of gastric acidity following gastro-enterostomy in some cases may be greater than that which occurs when achlorhydria fails to develop after partial gastrectomy. This apparently holds true regardless of the amount of stomach removed, short of total gastrectomy. In comparing the relative emptying time of the remaining por-

tion of the stomach following partial gastrectomy with that when the stoma is functioning properly following posterior gastro-enterostomy it would appear that in this respect the one operation is not superior to the other. When, however, direct anastomosis of the gastric remnant and the duodenum (Billroth I) has been made there is an apparent "hold up" or delay caused by duodenal penastaltic activity which does not occur following the Polya type of procedure.

The problem of whether or not gastric resection should be performed seems to concern duodenal ulcer only not gastric ulcer for morphologically and biologically the two differ greatly. The possibility of carcinomatous changes occurring in gastric ulcer and the small likelihood of their occurring in duodenal ulcer is well known. Similarly different results follow similar operations used in the treatment of these separate lesions. Almost never does recurring ulcer follow such procedures as (1) excision of a gastric ulcer and gastro-enterostomy or (2) partial gastrectomy for gastric ulcer.

In short, the surgical problems of today as applied to duodenal ulcer seem principally concerned in the selection of a procedure which will sufficiently reduce the acidity of the stomach and increase the rapidity of gastric emptying at a low risk. Since gastric and duodenal ulcers differ morphologically and biologically the problems presented are not parallel. The case for subtotal gastrectomy with removal of the duodenal ulcer remains one for further study during which time gastro-enterostomy should continue to hold a position of high regard for it will give good results at low operative risk in properly selected cases in which the response to a properly carried out medical regimen has been inadequate.

WALTMAN WALTERS.

<sup>1</sup>Symposium: Physiological studies subsequent to gastric operations for ulcer. *Proc. Acad. Medicine of Mayo Clinic* 1934. 447-51.

<sup>2</sup>Kline, Eugene, Archer, F. H. and Cohen, B. S. The end results of partial gastrectomy for primary gastric and duodenal ulcers. *The Ann. Surg.* 1932, 94: 242.

# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

THE book by Colwell and Russ entitled *X-Ray, Radium, and the Living Cell*, written nearly twenty years ago and revised in 1924, is well known to radiologists the world over, having served as the standard textbook in the English language on the physical, radiological, and pathological aspects of the influence of X-radiation on human tissues. The present publication<sup>1</sup> is a natural complement to the previous monograph, providing a well summarized compilation of the world's literature concerning all kinds of injuries from exposure to X-rays, γ rays, and other radio-active substances. No attempt has been made to give a complete account of such injuries, for that would require a large volume. The authors have presented the more outstanding features of these injuries, their prevention, and treatment, for the assistance of physicians and surgeons in general but especially for those beginning the study of radiology. It cannot be emphasized too strongly that every worker in radiology should do everything possible to familiarize himself with the pages of this work. Even though there may be encountered an occasional case of true idiosyncrasy, and though an occasional error of judgment may result in injury, the great majority of accidents may be prevented. The reviewer strongly advises the acquisition of this book by every physician who does radiological practice.

JAMES T. CASE

A COMPLETE treatise on osteomyelitis by Wilensky<sup>2</sup> gives the historical data concerning the condition and covers the methods of treatment from early history to the present day. The different bones are discussed from the standpoint of anatomy—gross and microscopic—and as to physiology. The question of blood supply is well covered, the author believes that thrombus embolus formation is largely responsible for the spread of osteomyelitis. The bacteriology of osteomyelitis is covered in detail, particular attention being paid to the type and mechanism of infection. The pathology, symptoms, differential diagnosis, X-ray findings, and treatment of the various forms of the disease—the primary and extension forms, the hematogenous, and the chronic—are aptly discussed. Osteomyelitis of the skull, sinuses, jaw, and many other bones, is considered, so that in all the book covers the subject of osteomye-

litis completely and thoroughly. It is the opinion of the reviewer that the book is the outstanding classic in the early and modern history of the condition.

JAMES J. CALLAHAN

VOLUME VII<sup>3</sup> of the *Practitioners Library of Medicine and Surgery* is a first printing and deals with the subject of pediatrics. It has an index, a good list of references at the end of each chapter, and it is fairly extensively illustrated. Most of the contributors are eastern pediatricists. Of the 34 authors, 2 are midwestern, 2 far western, and 2 southern.

The volumes of the *Practitioners Library*, at least at present, cannot be purchased separately—a wise provision since no volume of the system is entirely complete in itself. As stated in the preface, because of the duplication of some disease conditions in children and adults, it is impossible to avoid duplication. The editors have succeeded, however, in bringing such duplication to a minimum. For the most part, the duplication is apparent only as nice differences are drawn between the manifestations of a given disease in adult and child. For example, in Volume VII the subjects of polycythemia, leucocytosis, and leucopenia are only briefly touched on but are discussed fully in Volume II, while brachial palsy, although a neurological disturbance, is so distinctly pediatric that it is discussed fully. Such conditions as *pubertas præcox* and *eunuchoidism*, etc., are merely mentioned in this volume but are discussed fully in the section on endocrinology in Volume III. Non diabetic ketosis, however, largely a peculiarity of childhood, is taken up in great detail.

The subjects of feeding and conditions due to defective nutrition and infectious diseases are given special attention. Considerable importance is attached to diarrheal diseases and injuries of the newborn, conditions due to water and electrolyte imbalance (dehydration, etc.), neurological attitudes, and tuberculosis. Mental hygiene, child guidance, and recognition of behavior attitudes, the most recent addition to pediatric practices, are emphasized when necessary—the psychic and behavior aspect of the enuresis problem is well handled. The newer and most generally accepted classification of nephritis is followed in the chapter on renal disturbances. A progressive innovation is the discussion of rheumatic fever and chorea under or following the sections on heart rather than under infections and neurology, respectively, as in most texts. Infant

<sup>1</sup>THE PRACTITIONERS LIBRARY OF MEDICINE AND SURGERY Vol VII  
—PEDIATRICS New York and London D Appleton Century Co 1935

<sup>1</sup> X-RAY AND RADIUM INJURIES PREVENTION AND TREATMENT. By Hector A. Colwell, M.B. Ph.D. M.R.C.P., D.P.H. and Sidney Russ C.B.E. D.Sc. F.Inst.P. London Oxford University Press 1934.  
<sup>2</sup> OSTEOMYELITIS ITS PATHOGENESIS, SYMPTOMATOLOGY AND TREATMENT. By Abraham O. Wilensky, A.B. M.D. F.A.C.S. New York. The Macmillan Co 1934.

feeding is discussed under general principles and no particular food or formula is emphasized over other equally good ones. A valuable feature is a section on the antidotes for the common poisons found in the medicine chest.

Volume VII is intended as a guide to pediatricians for the busy practitioner and it is well written from this viewpoint.

JOSEPH K. CALVIN

THE researches of the various investigators in the report of the Imperial Cancer Research Fund for 1933-1934, constitute interesting and valuable additions to our knowledge upon these subjects and they have been carried out with the scientific accuracy characteristic of the workers. The conclusions upon the question of the mode of action of radiation are of special interest because of the difference of opinion that still exists upon the subject.

Experiments conducted histological studies on filterable tumors of the foal with special reference to metastatic growths and found individual characteristics in different strains and also close parallels with human tumors. In thymus, peritoneum, muscle, and kidney he observed proliferations of the invaded tissues comparable with the collateral hyperplasias of human tumors. It was also demonstrated that different tumor strains have distinguishing characteristics of growth and dissemination which are retained indefinitely. When part of the thymus of the foal is removed, minced, and re-implanted into the breast of the same bird, there is, first, necrosis involving particularly the thymocytes. It is quite evident that the potentialities of thymic epithelium are completely realized only under abnormal conditions.

Watson studied the effect of tar cancer in mice maintained on diets supplemented with fresh liver and found an increased carcinogenesis in such animals. This was indicated by the earlier appearance of benign warts and also the fact that larger numbers of animals developed benign and malignant skin lesions. On the other hand, the average interval of time between the first tar treatment and the development of malignancy was not reduced when the diet was supplemented with fresh liver. These experiments suggest that the development of benign hyperplasia and the subsequent development of malignancy are conditioned at least partly by different factors. Watson also observed an increased tumor response when the amounts of liver fed are varied within wide limits and also when the administration of liver is delayed until the sixth week of tar treatment. The factor or factors in fresh liver responsible for the increased response are comparatively heat-stable.

Horsing conducted macroincubation studies of tar tumors. By means of excellent and striking photomicrographs it is demonstrated that detailed comparison can be made between the ash of the

hypertrophied tarred skin and that of the carcinoma cells in their varying stages of differentiation. A further study is reported by the same author upon the action of radium on the inorganic structure of tumor cells. The maximum increase of mineral salts occurs on the sixth day following irradiation.

Crabtree and Cramer deal with the action of radium upon cancer cells. These authors concluded that susceptibility to radium is not a fixed property of a given cell, but varies with its environment. Anaerobiosis, hydrocyanic acid, and cold diminished the functional activity of the respiratory mechanism, but the effect on the susceptibility to radium is not the same. Anaerobiosis diminished susceptibility to radium whereas hydrocyanic acid and cold increased susceptibility to radium. In third paper by these authors, the conclusion is drawn that  $\gamma$  rays have the same biological effect on cancer cells as  $\alpha$  rays as a mixture of  $\beta$ - and  $\gamma$ -rays. Under both circumstances the functional state of the respiratory mechanism determines the biological response of the cell. In the following paper Cramer found that spontaneous mammary carcinomata of the mouse show considerable differences in their sensitivity to radium. No evidence was obtained to indicate a stimulation of growth or enhanced metastatic dissemination by radium. The process of regression of the radiosensitive tumors is believed to be due to damage inflicted on both the tumor and the tumor bed. In the radioresistant tumors irradiation does not produce macrophage invasion. The ability to bring about the local disappearance of a malignant new-growth by an agent which does not kill all the malignant cells directly suggests to the author the possibility of a systemic treatment of cancer along the same lines.

The last two papers are by Ludford. By means of excellent dark ground photographs distinguishing features are demonstrated between tumor cells and associated macrophages and fibroblasts. A new method of staining fatty substances in living cultures is presented. It is suggested that the plasma membrane of malignant cells is relatively rich in fatty substances.

M. C. CORNIA

IN his book of 300 pages Dr. Goldscheider has attempted to cover not only the pathological physiology, diagnosis, and treatment of the glands of internal secretion but also to discuss their influence in disorders of nutrition, organic and mineral metabolism, infection, locomotion, psychiatry, ophthalmology and dermatology. This is almost too ambitious a task. The bridge of hypothesis in many relationships studied becomes so great that endocrinology is discredited rather than enlarged.

The presentation is made as a personal offering without review of the work of others. This is interesting and valuable but statements of results should then be accompanied by some data indicating the experience back of the claims made. For instance,

diiodotyrosin, recommended for the medical treatment of hyperthyroidism following the work of Abelin at Bern, to whom no reference is made, is represented as being "the biological antagonist to thyroxin" and a "satisfactory antidote to thyroxin." This claim has not been substantiated by others attempting to corroborate Abelin's work. It is unfortunate for endocrinology that any false hopes should be raised. A rather specialistic bias is also suggested by the introduction which states that "an underlying veiled endocrinopathy should be suspected in all cases in which the symptoms observed are not satisfactorily explained on the basis of demonstrable pathological changes." Would it not be just as valuable to consider an underlying veiled infection, malignancy or neurosis?

If the book were an informal discussion based on the author's extensive personal experience it would be welcomed by students of endocrinology, but in its present form as an authoritative guide to practical endocrinology it fails of its objective.

PAUL STARR.

THE book<sup>1</sup> of Lockhart-Mummery is not an encyclopedic treatise on the surgery of the rectum and colon but records the author's own experience and very largely voices his own opinion on the subjects. In this edition are emphasized particularly aseptic technique, improved methods of anesthesia and rational methods of after-treatment of rectal operations. The chapter on diverticulitis is especially good.

Almost every reviewer takes exception to certain omissions or commissions in a book under scrutiny, and I would therefore call in question the omission of any mention of lymphogranuloma inguinale as a cause of rectal stricture. The statement that the operation of choice in severe ulcerative colitis is without doubt appendicostomy, would be skeptically received in this country where proctostomy is done with the purpose of sidetracking the fecal stream from the ulcerated colon.

The author very properly classes the injection treatment of hemorrhoids as palliative and says that danger lies in its use by those who have no special knowledge of the differential diagnosis of rectal lesions.

In discussing prolapse of the rectum, he states that the condition usually corrects itself in children if the nutrition and habits of elimination are properly regulated.

As Dr Mummery has been an ardent advocate of perineal resection of the rectum for carcinoma after preliminary colostomy, one is not surprised to have the safety of the operation emphasized but rather questions the statement that "there is no doubt that the proportion of cures on a 5 year basis is higher than with any other method." In his own series of cases, he has a 4 per cent mortality and a

52 per cent 5 year cure. In the abdominoperineal operation, the mortality in his hands is 15 to 30 per cent.

In general one can highly recommend the book as containing much sound advice and wisdom, especially as it concerns itself with the treatment of lesions of the rectum.

VERNON DAVID

THE last volume, XII, together with the index of the *Cyclopedia of Medicine*<sup>2</sup> is now available. It is well to recall that Dr George M. Piersol is editor-in-chief and he selected a group of associate editors to assist in this big task of arranging the whole field of medical endeavor into an alphabetical system. The material has been supplied by other associates selected because of their pre-eminence in their specific fields of medicine and medical sciences not only from most of the great medical schools of the United States and Canada but also from many of the countries of Europe, Central and South America. The volumes are of convenient size (7 by 10) of 700 to 800 pages, in attractive flexible green bindings. The material is well printed on substantial paper. The disease entities have been discussed in an orderly way from the standpoint of etiology, pathology, symptomatology, differential diagnosis, and treatment. The operative technique together with pre-operative and postoperative management has been emphasized in the care of the surgical disorders, gynecology, obstetrics, ophthalmology, and otolaryngology.

The twelfth and last volume has for its first topic, "Tendons, surgery of," and ends with "Zingiber, its preparations, doses, physiologic action and therapeutic uses." The index of 475 pages is to be replaced with each annual supplement which Dr Piersol plans to bring out to cover the rapid advances and constant changes taking place in medicine.

M HERBERT BARKER.

THE text entitled *Modern Operative Surgery*,<sup>3</sup> edited by G. Grey Turner, should at once become the outstanding book in its field. Written by a most formidable group of English surgeons, uniting in an effort to present an authoritative survey of the whole range of modern surgical operations, it covers its purpose excellently. Aimed to appeal primarily to the surgeon, it not only gives the detailed technique of modern operations, but offers also the choice of operation as well as the preparation and after-treatment of the patient so necessary to a happy result. One statement in the editor's introduction—"the proper operation clumsily performed is much more likely to be successful than the wrong operation however brilliantly executed"—portrays the aims of these British surgeons.

Several of the chapters are of necessity brief, but with few exceptions deserve especial commendation.

<sup>1</sup>THE CYCLOPEDIA OF MEDICINE. Edited by George Morris Piersol B.S. M.D. and Edward L. Bortz A.B. M.D. Vol. XII and Index Philadelphia F. A. Davis Co., 1934.

<sup>2</sup>MODERN OPERATIVE SURGERY Edited by G. Grey Turner M.S. F.R.C.S. (Eng.) F.A.C.S. (Hon.) Vols. I and II 2d ed. Baltimore William Wood & Co. 1934.

<sup>3</sup>DISEASES OF THE RECTUM AND COLON AND THEIR SURGICAL TREATMENT By J. P. Lockhart Mummery, F.R.C.S. (Eng.) M.A., M.B. B.C. (Cantab.) 2d ed. Baltimore William Wood & Co. 1934.



The two chapters by W. Sampson Handly on Principles of the Operative Treatment of Malignant Disease, and Operations on the Breast, are noteworthy examples and should be of particular interest to all medical men so significant is the material contained within. One of the masterpieces is the chapter on Operations on the Stomach, as revised by A. J. Walton. Walton's experience is perhaps second to none and this knowledge is adequately reflected in his chapter on gastric surgery.

Too much cannot be said for these two volumes on operative surgery for it would mean repeating again and again. Every field of surgery is covered, and covered unusually well. Each chapter is significant. Both volumes are profusely illustrated. *Modern Operative Surgery* will meet instant and heartfelt approval by every surgeon, for it bridges a tremendous gap which heretofore has remained unattended.

KARL I. GREENE

THE three hundred page monograph, which is the third part of Volume VIII of *Viet Handbuch der Gynäkologie* dealing with infections of the female genitalia, is devoted to a consideration of gonorrhea. The attempt has been made to have this volume encyclopedic and all inclusive, as are the other volumes of this *Handbuch*. A tremendous bibliography of thirty-six closely printed pages is therefore included, thus making it too cumbersome for the average reader.

This volume is for the most part sketchily written. One suspects that it is simply an enlarged edition of the author's previous monograph which appeared independently in 1913. It is difficult to understand why only three pages are devoted to gonorrhea and pregnancy. The reader will be surprised to find that such procedures as multiple puncture of the cervix and intrauterine cervical massage are recommended for the treatment of endocervicitis; on the other hand, cervical cauterization is not even mentioned. The work is not well illustrated and one is forced to the conclusion that this volume is definitely not keeping with the other volumes of this *Handbuch* which have appeared to date.

RAIMUND RIZEN

THE outline of the treatment of fractures by Spence is well written, contains many useful and helpful illustrations, and is particularly adapted to those who are desirous of sufficient knowledge for the treatment of fractures, without extensive reading.

It is a compact, interesting book, describing all of the important fractures and dislocations. The treatment of each fracture is briefly discussed.

In my opinion this small fracture book is an excellent outline for the general practitioner.

JAMES J. CALLAHAN

Viet's HANDBUCH DER GYNEKOLOGIE. Edited by W. Stöckel and ed. of VIII part. One hundred and thirteen pages. GUSTAV FISCHER, 25 C. Bismarck, Munich. J. F. Bergmann, 1914.

BRUCE GUTHRIE'S A MODERN TEXTBOOK OF FRACURES. By H. W. B. SPENCE, A.B. M.D. Baltimore: Williams and Co. 1913.

THE enthusiastic reception and almost immediate success of McGregor's *Synopsis of Surgical Anatomy* make one look with pleasurable anticipation into the second edition, enlarged by the addition of numerous valuable sections. McGregor's book is an innovation in surgical anatomy and presents, rather than a systematic exhaustive treatise on anatomy, a series of separate essays each complete in itself, and often dealing with diverse regions and systems.

The book is divided almost equally into two halves—one dealing with normal anatomy the other termed Anatomy of the Abnormal, including such varied subjects as the anatomy of congenital errors, the anatomical bases of various clinical tests, and of surgical procedures and approaches. The student may miss the usual amount of anatomical material presented in the usual textbook of surgical anatomy but this lack is more than compensated for by the great wealth of practical and important surgical information.

Although the book is labeled a synopsis, I feel this is somewhat of a misnomer, since in no way can its brevity be confused with inadequate or outline presentation. Subjects, as presented, are logically and thoroughly treated, explanations are satisfying and readable. The book is wholeheartedly recommended to student and practitioner alike.

MICHAEL L. MCGEE

THE second edition of Dr. Babcock's *Textbook of Surgery* should find great favor among students of surgery. The simplicity and orderly presentation which contributed largely to the popularity of the original volume have not suffered at the expense of additional text and many new illustrations. Only surgeons of Dr. Babcock's wide experience could discuss accurately such a great variety of surgical conditions as may be found in his book. The reader will be impressed with the fine illustrations of operative procedures, he will particularly enjoy the chapters on fractures, anesthesia, and surgery of the endocrine glands. The many advances in surgery which have taken place since the publication of the first edition have been adequately considered in the second edition. Dr. Babcock's keen powers of observation and surgical originality stand out on every page.

The first book was distinct success; the revised edition should prove even more popular.

FREDERICK CHRISTOPHER

TEACHERS of roentgenology are always on the lookout for good textbooks that present the subject of roentgenological diagnosis in terse, attractive English, illustrated adequately by actual roentgenograms. It is somewhat new departure to find a

A SYNOPTIC SURVEY OF RADIOLOGY. By Alexander Lee McGregor, M.D. (Edin.), F.R.C.S. (Eng.). With foreword by Sir Harold E. S. F.R.C.S. (Edin.) and Ed. Baltimore: Williams and Co. 1914.

A TEXTBOOK OF RADIOLOGY FOR STUDENTS AND PRACTITIONERS. By Wayne Robinson, A.M. M.D. LL.D. B.A.C.S. Ed of Philadelphia and London: W. B. Saunders Co. 1913.

book, such as Bull's *X-Ray Interpretation*<sup>1</sup>, which answers to most of the above conditions but in which the 280 original illustrations are all line drawings or silhouettes in place of the usual half-tone reproductions of the original roentgenograms. At first this seems to be a fault until we reflect that many of the works in which roentgenograms are used as illustrations have accompanying diagrams or outline drawings of an explanatory character. For most purposes it will have to be admitted that these line and silhouette drawings answer the purpose of illustration admirably. In the chapter on the head, however, there is a definite lack of satisfactory illustrations and especially in that portion which deals with brain tumors and particularly with the sinuses. Again, in the lungs much of the refinement of X-ray illustration is lacking in the simple outline drawings. Here again, it must be admitted that for instruction purposes these line drawings have considerable value.

As a textbook the work proves to be quite suitable. It devotes more space to common pathological conditions than to rare ones, and much prominence is given to the normal, for it is quite truly stated that no accurate conception of the pathological is possible without a knowledge of the normal.

JAMES T CASE.

IN *Blood Groups and Blood Transfusion*<sup>2</sup>, Wiener has attempted to condense all the present day knowledge concerning these subjects into a book of two hundred pages and has succeeded remarkably well.

The first third of the book deals with the blood groups as we know them clinically. Many enlightening facts are brought out concerning the technique of blood grouping and the sources of error. He advocates strongly the more general use of the international nomenclature for the blood groups, and points out that many transfusion accidents have been the result of confusion between the Jansky and Moys numberings. This section is well written and very instructive to the clinician and particularly to technicians.

The second section deals with the indications for blood transfusion and the various techniques employed in their performance. This is a review of our present knowledge and while complete does not offer anything new.

The author next deals with the heredity of the blood groups and gives an exhaustive review of the present day knowledge of this subject. This section is of particular value to one interested in this subject.

The next portion deals with the various subgroups of the four standard groups and the author points out that eighteen distinct types of human blood may be identified. He also brings out the fact that there are group specific substances in the various organs and fluids of the body.

In the chapter dealing with the anthropological investigations of the blood groups, the differences in animal blood are discussed, as are blood groups and their relation to clinical medicine.

In the last chapter, Wiener discusses the medico-legal aspect of blood groupings and cites many interesting cases. He shows that the blood groupings have been of inestimable value in establishing non-paternity, in identifying babies, and identifying criminals. He advocates a more widespread use of this knowledge.

The entire book is well illustrated and contains much detail as to technique. It should prove very useful as a ready reference on this subject.

BERTRAM J. FITZGERALD

THE impressive work<sup>1</sup> on roentgentherapy by Perussia, one of the collection of monographs and treatises on biology and medicine edited by Dr Prof Carlo Foa, constitutes a complete treatise on radiotherapy, comparable to similar treatises in German. There is none in English or French which is at all comparable. It would be a blessing if some one would arrange for the production in English of a work of this type. The scope of the two volumes may be inferred from the closely printed sixteen hundred large pages from which the authors have sought to eliminate all matters of purely historical or academic interest. That nothing of importance has been omitted is due to the plan of the work, Italian specialists dividing among themselves the various fields of radiotherapy and presenting them in complete fashion.

Volume I is devoted to the basic physical and biological principles constituting the foundation of radiotherapy, including the modern physical theory of radiations, a review of apparatus, dosimetric methods, and means of protection. The section by Gallavresi on the fundamental biological effects of radiations is especially attractive. Volume II considers the applications of radiotherapy. Each chapter is followed by an excellent bibliography of the important works consulted by the authors or recommended for further reference.

When one realizes the vast mass of information available for those who dedicate themselves to the clinical application of radium and roentgen rays it is not possible to escape a feeling that the physician or surgeon who makes an occasional application of radium without having had at least some fundamental education in radiology displays a remarkable temerity. It would be wonderful if all such could read the 110 pages of this work on reactions and injuries from radiotherapy.

There would be fewer implantations of radon and radium seeds and needles and greater use of radium and radon packs applied at a distance of 10 centimeters or more and the higher voltages of roentgen therapy with thick filters if a better appreciation

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of radiation effects obtained among the surgeons and gynecologists. The law of the inverse square holds good just as much in estimating the effects of a minute radon seed as for a large radium pack or a high voltage roentgen tube.

JAMES T. CASE

IN his preface, Barbour states the purpose of this book is, first, to present to physicians a concise, practical, and systematic method of prescribing diets and applying treatment by diet to health and disease; second, to aid the physician and dietitian in teaching the individual patient how to make selection of the proper amount and type of food that has been prescribed for him. The purpose has been accomplished exceedingly well.

The work is divided into five sections the first of which deals with the *dietetic requirement of healthy individuals*. The second section has to do with the general application of diet to disease. Here are the principles of calculating any diet for any patient and of applying the calculated diet. Servings are described in a manner that will remove much of the uncertainty that usually attaches to that term.

The third section, and major portion of the book, is devoted to diet in disease. Here are discussed, first, the diseases in which diet is of paramount importance and, second, diseases in which diet is of varying importance. Specimen diets are abundant and one will find diets for every disease, the variations and complications of every disease in which diet plays a part. It must be remembered that the book is devoted to dietetic treatment. If one wishes to learn, for instance, about diabetes mellitus, part from the diet, one must look elsewhere. But if one wishes to know about the dietetic treatment of diabetes, or if it is medical or surgical complications, one will find it here. The same is true of any disease in which dietetic treatment is of importance.

It is possible that the work will receive criticism from some quarters, but the criticism must be over controversial points. There might be objection, for instance, to the recommendation of low protein diet in all forms of heart disease. The failure to mention the alleged value of the high protein diet in pre-operative preparation for gastro-intestinal surgery might be commented upon but on the whole little adverse criticism may be justifiably offered.

The fourth and fifth sections deal with hospital diets, weight charts, tables, and similar supplementary material.

This book will make valuable addition to the armamentarium of any physician. For the physician who is unfamiliar with the finer principles of dietetic treatment it will furnish a simple and understandable guide to this form of treatment of disease. For the dietitian and for the physician who must direct the diet of his patients, there is wealth of material in the way of easily understood and well constructed diets to meet almost every need.

G. K. F.

THE monograph by James C. White, of Boston, entitled *The Autonomic Nervous System* is a splendid contribution to this fragment of medical study and practice. This is the second American contribution in this field, W. K. Livingston having published a few months previously monograph covering much the same material, entitled *The Clinical Aspects of Visceral Neurology*. These publications emphasize the growing importance of an appreciation of the autonomic nervous system in the practice of both medicine and surgery and reflect great credit on the American workers in this important field.

Both by training and experience Dr. White is eminently qualified to write concerning this matter. His surgical background was largely in the realm of experimental physiology and his acquaintance and intimate association with Professor René Leriche at Strasbourg gave him, years ago, added impetus to study the autonomic nervous system. At the Massachusetts General Hospital, Boston, he has had large clinical experience which has permitted him to amplify his experimental physiological studies and apply to man the most recent concepts of the physiology of the autonomic nervous system. Thus, his book represents clinical experience based upon the most modern physiological work.

Dr. White's contribution covers the whole matter in most orderly fashion. It begins with the fascinating story of the historical background leading to the development of our modern knowledge. Then follows a complete, well illustrated, and admirably presented summary of the anatomy and physiology of the autonomic nervous system. The next chapter deals with the several methods by which the autonomic nervous system may be studied. Here follows one of the chief values of this contribution—that it gives in detail the methods by which one may now evaluate signs and symptoms in patients as to their alterations in the normal physiology of the autonomic nervous system. The standardization of certain tests has always been a chief contribution to the development of our knowledge in any field, and in this field in particular. Here until recently so much depended upon impression rather than upon measurable findings, it is important that we have definite tests that may both measure alterations in function before and after operation, as well as give to individual observers data which can, in part at least, be compared to results obtained by other observers. Then follow chapters dealing with the rôle played by the autonomic nervous system in peripheral vascular disease, pain, in hypertension, and in the special disorders of the brain, heart, aorta, lung, gastro-intestinal tract, and urogenital tract. The concluding chapters, which are devoted to the operative procedures themselves, will be of chief value to the surgeon, for here he will find outlined and well illustrated the technical steps now

proposed for assisting in the treatment of those disorders in which the autonomic nervous system is involved

It would be quite unfair, however, to look on this monograph as a book only for the surgeon, for its physiological data and clinical discussions of conditions are equally important to all workers in the field of medicine. It is a very complete summary of knowledge today in this important field, and it should be of great practical value—

1 Because of its admirable presentation of acceptable tests,

2 Because of its excellent discussion of disorders in which the autonomic nervous system is involved,

3 Because of the wealth of clinical material that supports the suggestions and conclusions, and

4 Because of the careful presentation of the actual surgical procedures to be performed

ELLIOTT C. CUTLER.

THE little book<sup>1</sup> by Frederick Watson on the life of Hugh Owen Thomas can be read in an hour and a half, and will furnish most interesting reading. The author is the son-in-law of Sir Robert Jones, who was Hugh Owen Thomas' nephew, apprentice, assistant, and successor, so that its contents are authentic. It is written in a clear, readable style.

To Frederick Watson the profession is indebted for the recording of the life of this most interesting man, who, born in a family of bone setters, became practically the pioneer of modern orthopedic surgery. He revolutionized the treatment of tuberculous joints and laid the foundation for most of the principles of modern orthopedic surgery exclusive of the purely surgical technique.

Thomas was practically unrecognized in his own city and country until after his death. He established the most famous shrine of orthopedic surgery, 11 Nelson street in Liverpool, which has attracted so many of the younger and older orthopedic surgeons of America. A frail, little man, he carried on for 30 years, the arduous general practice among the poor of the Liverpool dockland, without ever taking a holiday and without the advantage of a hospital appointment.

There is an interesting section in the book concerning our own John Ridlon who practiced orthopedic surgery for 45 years and is now, at the age of 85, in retirement in Newport, Rhode Island. When Ridlon read Thomas' book he hastened to Liverpool and as he handed his card to Hugh Owen Thomas, said "Mr Thomas, I have read your book on the hip, ankle, and knee, and I have come over 3000 miles to find out whether I am a fool or you are a liar."

One of the greatest things Sir Robert Jones ever did was to make the main principles of Hugh Owen Thomas acceptable to the medical and surgical profession. Like the work of Sir Robert Jones and Lister, the work of Hugh Owen Thomas was appre-

ciated in other countries, particularly in America, before it was in England.

PHILIP LEWIS.

VOLUME VIII of *The Practitioners Library of Medicine and Surgery* is composed of monographs from the pens of 35 different contributors who have a special knowledge in the field upon which they write. These authors, however, do not lose sight of the fact that they are speaking in the main to the general practitioner. Technical procedures requiring highly specialized skill are omitted, preference being given to fundamentals of therapeutics as applied to the ordinary patient which are discussed in minute details and the principles involved are explained. This book begins where a book of therapeutics should, with the care of the patient as an individual and ample space is given to the principles involved in diet, hydrotherapy, climato-therapy, physical therapy, vaccine and serum therapy, non specific protein therapy, and psychotherapy, which are so often neglected in general textbooks and in consequence are so frequently used without an adequate understanding of their uses, limitations, and contra indications. Three fourths of the book is devoted to special therapy of specific conditions and a wealth of information is compressed within the pages. Most of Fantus' *Technique of Medication*, with innumerable useful suggestions, is included in this volume, in itself an asset to any book on therapeutics.

HOWARD B. CARROLL.

THE present fasciculus<sup>2</sup> of the Paire, Giraud, and Dupret *Surgical Anatomy* deals with the small and large bowel, exclusive of the duodenum and of the anus. Each section is taken up in great detail, beginning with a succinct discussion of the embryological development of the particular segment of bowel under consideration. This provides an excellent background for an understanding of the normal anatomical conditions, as well as for the numerous variations which are so frequently present. Surgical applications are reduced to the discussion of well based principles which have stood the test of time. Long descriptions and illustrations of operative procedures have been dispensed with, and in their place are found stimulating drawings and text matter describing the anatomy and indicating the basis for operative procedures.

The book is divided into eight sections: (1) the great omentum, (2) the mesentery and small bowel, (3) the large bowel as a whole, (4) the cecum and appendix, (5) the right colon, (6) the left colon, (7) the ileocecal colon, (8) the rectum. The book is the outcome of considerable patient labor, both on the living body and the cadaver, and is excellently illustrated by 594 line drawings. It should be of great help and a stimulus to the thinking surgeon.

MICHAEL L. MASON.

<sup>1</sup>THE PRACTITIONERS LIBRARY OF MEDICINE AND SURGERY. VOL. VIII.—THERAPEUTICS. New York and London: D. Appleton Century, 1935.

<sup>2</sup>PRATIQUE ANATOMO-CHIRURGICALE ILLUSTRÉE. BY F. Paire, D. Giraud, and S. Dupret. Fascicule II.—RÉGION ABDOMINALE MOYENNE ET RECTUM. Paris: G. Doin et Cie, 1935.

<sup>3</sup>HUGH OWEN THOMAS: A PERSONAL STUDY. By Frederick Watson. London: Oxford University Press, 1934.

## BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

**GYNECOLOGY FOR STUDENTS AND PRACTITIONERS** By T. Watts Fden, M.D., C.M. (Edin.), F.R.C.P. (Lond.) F.R.C.S. (Edin.), F.C.O.G. and Colthbert Lockyer M.D. B.S. (Lond), F.R.C.P. (Lond), F.R.C.S. (Eng.), F.C.O.G. 2th ed. by H. Beckwith Whitehouse, M.B., M.S. (Lond) Ch.M. (Birmn), F.R.C.S. (Eng.), F.C.O.G. F.A.C.S. (Hon.), London. J & A Churchill Ltd. 935.

**CHRONIQUE DE LA TUBERCULOSE PULMONAIRE, INDICATIONS, TECHNIQUES, RÉSULTATS** By A. Bernon and H. Fruchard. Paris. G. Doin & Co., 935.

**THE PRINCIPLES AND PRACTICE OF MEDICINE** By the late Sir William Osler M.D. F.R.S. and Thomas McCrea, M.D. 2th ed. compl. rev. New York. D. Appleton-Century Co. 935.

**THE TREATMENT OF FRACTURES** By Dr. LORENZ BOKER. Fourth English edition, translated from the fourth enlarged and revised German edition by Ernest W. Hey Groves, M.S. M.D. F.R.C.S. Baltimore. Williams Wood & Co. 935.

**YOUR NEW BABY; HOW TO PREPARE FOR IT AND CARE FOR IT.** By Linda McClure Woods, R.N. With a foreword by Sterling Ruffin, M.D. New York. Robert M. McBride & Co. 935.

**APPARATUS AND TECHNIQUE FOR ROENTGENOGRAPHY OF THE CHEST** Charles Weyl and S. Rind Warren, Jr. Springfield, Ill. and Baltimore, Md. Charles C. Thomas, 935.

**ELECTROTHERAPY AND LIGHT THERAPY.** By Richard Kervick, M.D. 2th ed. thoroughly rev. Philadelphia. Lea & Febiger. 935.

**INJURIES AND THEIR TREATMENT** By W. Eldon Tustin, M.A. B.Ch. (Cantab.) F.R.C.S. (Eng.) New York. Oxford University Press, 935.

## ANTERIOR GASTRO-ENTEROSTOMY BY THE SHORT LOOP METHOD

## A Correction

IN the article by Dr. Clarence E. Rees, entitled "Anterior Gastro-Enterostomy by the Short Loop Method," which appeared in the June, 1935 issue, p. 115, an error appears in the second sentence of the fifth point of the technique. The sen-

tence should read: "Then the remainder of the opening in the transverse mesocolon is closed by suturing it to the stomach proximal to the clamp." The word "mesocolon" should be substituted for "colon."

# CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

ROBERT B. GREENOUGH, Boston, *President*

DONALD C. BALFOUR, Rochester, *President-Elect*

HOWARD C. NAFFZIGER, *Chairman*, THOMAS F. MULLEN, *Secretary*, *Committee on Arrangements*

## THE 1935 CLINICAL CONGRESS IN SAN FRANCISCO AND OAKLAND

THE Committee on Arrangements for the twenty-fifth annual Clinical Congress of the American College of Surgeons to be held in San Francisco and Oakland, October 28-November 1, is assured of the hearty co-operation of the clinicians at the two medical schools and twenty-seven hospitals that will participate in the clinical program, and plans to provide a program of surgical clinics in the hospitals and medical schools of that great medical center on the Pacific coast that will present a complete showing of their clinical activities in all departments of surgery.

The clinical program, published in tentative form in the following pages, will be further revised and amplified during the coming weeks as the work of the program committee progresses. It will be noted that operative clinics and demonstrations in the hospitals are scheduled for the afternoon of Monday, October 28, beginning at 2 o'clock, and for the mornings and afternoons of each of the four following days.

Special features of the clinical program include (1) Cancer clinics demonstrating the treatment of cancer by surgery, radium and X-ray, (2) fracture clinics demonstrating modern methods of treatment, (3) clinics in traumatic surgery demonstrating the newer methods of rehabilitation of injured patients by surgery and physiotherapy.

The sub-committee in charge of the section on surgery of the eye, ear, nose and throat, in addition to arranging for a series of ophthalmological and otolaryngological clinics and demonstrations in the hospitals and medical schools, is preparing programs for scientific sessions at headquarters on Tuesday, Wednesday, Thursday and Friday mornings at which distinguished specialists in these branches of surgery will present and discuss papers on subjects of clinical interest.

Surgical motion picture films, both sound and silent, will be exhibited daily at headquarters at the Fairmont Hotel. Such surgical film exhibitions

have met with popular acceptance in recent years, and an extensive exhibit, including many new films, is planned for this year's Congress.

### EVENING MEETINGS

The Executive Committee of the Board of Regents is preparing programs for a series of five evening sessions. At the presidential meeting on Monday evening in the Municipal Opera House the retiring president, Dr. Robert B. Greenough, of Boston, will deliver the annual address, and the officers elected at the 1934 Clinical Congress will be inaugurated—Dr. Donald C. Balfour, Rochester, president, Dr. Arthur W. Allen, Boston, and Dr. John A. Gunn, Winnipeg, vice-presidents. Also at that session Dr. George Crile will deliver the annual College oration on surgery.

Sessions on Tuesday, Wednesday and Thursday evenings will be held in the Auditorium of the Veterans' Building, at which eminent surgeons of the United States and Canada together with visiting surgeons from foreign countries will present and discuss papers dealing with surgical subjects of timely importance.

The annual convocation of the College will be held in the Municipal Opera House on Friday evening when the 1935 class of initiates will be received into Fellowship. The Fellowship address will be delivered by Dr. Robert Gordon Sproul, president of the University of California.

### SYMPOSIUM ON FRACTURES

The symposium on fractures will be held under the auspices of the College Committee on Fractures on Tuesday afternoon, in the Gold Ballroom of the Fairmont Hotel, with Dr. Frederic W. Bancroft, New York, presiding.

The chairman will present a summary of the activities of the committee including the accomplishments of its regional fracture committees throughout the United States and in Canada.

Among those presenting papers will be Dr. E. Payne Palmer Phoenix, on Highway First Aid Stations; Dr. Frederic J. Cotton, Boston, on Tender Fractures of the Knee; Dr. Clay Ray Murray New York, on The Status of Fractures in the Field of Surgery; and Dr. E. Dunbar Newell, Chattanooga, on Local Anesthesia in Fractures.

Demonstrations of approved methods of treating fractures will be conducted daily as a part of the scientific exhibit of the Congress.

#### SYMPOSIUM ON CANCER

The symposium on cancer, under the auspices of the College Committee on the Treatment of Malignant Diseases, will be held on Thursday afternoon in the Gold Ballroom of the Fairmont Hotel, with Dr. C. A. Dukes, Oakland, presiding.

The symposium this year will concentrate on standard accepted methods of treatment, though a report on 6-year results of therapy will be made from the Department of Clinical Research continuing the gathering of statistics on this subject from clinicians in various parts of the United States and Canada as in the several years past.

Among the papers to be presented on standard methods of treatment will be those of Dr. Benjamin S. Barringer New York, on Treatment of Cancer of the Prostate Gland; Dr. Alton R. Kligore, San Francisco, on Treatment of Cancer of the Fundus Uteri; and Dr. Frank E. Adair New York, on Treatment of Melanoma.

#### CONFERENCE ON INDUSTRIAL MEDICINE AND TRAUMATIC SURGERY

The Board on Industrial Medicine and Traumatic Surgery will hold its conference on Friday afternoon in the Gold Ballroom of the Fairmont Hotel, with Dr. Frederic A. Benley Waalegan, presiding.

A broad program of interest to those in various fields of industrial endeavor has been arranged. This includes papers by Senior Surgeon R. R. Sayers and Passed Assistant Surgeon R. R. Jones of the United States Public Health Service, Washington, on Silicosis and its Control; Dr. Sydney Walker Chicago, on Analysis of Five Hundred Intra-ocular Steel Operations; Dr. Adelbert Bettman, Portland, on Tannic Acid and Silver Nitrate in Burns; and Dr. Loyal A. Shoudy Bethlehem, on Heat Exhaustion.

A report will be made on the activities of the College in conducting investigations and surveys among industrial establishments during the past year in continuation of the work done along these lines during the past five years.

#### HOSPITAL CONFERENCE

The eighteenth annual hospital standardization conference will open with a session in the Gold Ballroom of the Fairmont Hotel at 10 o'clock on Monday morning at which addresses will be delivered by distinguished representatives of several organizations, each having a vitally important message for the assembly. At this session the annual report of the hospital standardization activities of the College for 1935, including the list of approved hospitals, will be presented.

Monday afternoon will be given over to a discussion of hospital problems from various aspects in which administrators, surgeons and others will participate.

Tuesday morning will be devoted to a "panel" discussion of the hospital's obligation to its community and its part in the community life professionally and economically.

A joint session with the Association of Record Librarians will be held on Wednesday morning at which problems concerning hospital records are to be discussed. This will take the form of a symposium and round table conference.

Tuesday and Wednesday afternoons will be devoted to definitely planned departmental demonstrations in hospital administration in certain of the San Francisco hospitals. These demonstrations will show how various departments function, affording those present an excellent opportunity to see how other institutions carry on their activities.

Thursday will be Oakland Hospital Day and a program of demonstrations of special interest will be carried on in four of the major hospitals in Alameda County with the co-operation of the Oakland Hospital Council, at which many new features and procedures in hospital management will be demonstrated.

Through the courtesy of Dr. D. W. Black, medical director of the Highland Hospital and director of Alameda County health activities, those who are interested in the Alameda plan will be given an opportunity to make an excursion through the county on Friday.

#### A VACATION ON THE PACIFIC COAST AND THE CLINICAL CONGRESS

Many Fellows of the College and their guests, who will attend the Clinical Congress in San Francisco in October, will plan to take advantage of the opportunity which naturally suggests itself to include a vacation on the Pacific coast. All the railroads are offering very low round-trip rates with liberal stopover privileges from all parts of the United States and Canada, with the added

privilege of traveling to the coast by one route and returning by another, thereby affording unusual opportunities for visiting many points of interest en route.

When nature fashioned the Pacific coast she was in a spendthrift mood. From the Canadian border to the Mexican line she scattered her beauties and wonders with a prodigal hand—mountains, rivers, waterfalls, oceans, beaches, forests, lakes, even a live volcano, the only one in the United States.

Few cities have so impressive a setting as San Francisco. The rugged hills upon which it is built, the Golden Gate, Mt. Tamalpais, the misty bay to the east, Oakland and Berkeley and the hills beyond, all contribute to its grandeur. It is a pleasing picture and the citizens of San Francisco have not been unmindful of it. Their parks and residence districts have a dignity and beauty in keeping with the scene about them.

The glamour of the city is inescapable, but no amount of description can picture accurately this unique city. One must see for himself how the many charming aspects of San Francisco and its environs blend into one delightful and unforgettable picture.

While on the coast one will naturally wish to see as much of the great west as possible and will find it surprisingly easy to visit the many "high spots" in a relatively short time and at a reasonable cost.

Along the Pacific coast one will find much to claim his attention. First, there is the California-Pacific International Exposition at San Diego—a World's Fair of magnitude, with many important medical and other scientific exhibits—erected in Balboa Park, a tropical fairyland. The buildings, which are permanent structures, have their dignity and beauty enhanced by the gorgeous setting.

Los Angeles with its mountain background, its broad boulevards, its nearby beaches, its hospitality—and Hollywood—afford opportunities for entertainment and recreation. A one-day trip to enchanting Catalina Island with its balmy south sea island atmosphere, would naturally suggest itself.

Traveling south but a short distance from San Francisco, one enters the San Joaquin valley at Merced—the gateway to Yosemite National Park, where one views one of the most famous spectacles of nature. The valley occupies but eight square miles, but in this limited space are gathered more natural wonders than can be found in any other similar area in the world. It contains eight waterfalls, the lowest twice the height of

Niagara, and the highest the equal of ten Niagaras. There are meadows of deep grass and wild flowers, a rushing mountain river, forests and towering cliffs. A short distance beyond is Sequoia National Park, containing thousands of giant Sequoia, the largest and oldest living things on the face of the globe.

Del Monte and Pebble Beach, on the famous seventeen mile drive, are but a short distance from San Francisco. Other nearby points of interest are Paso Robles, with its almond groves, lovely Santa Barbara with its famous Old Mission, and a score of cities whose names are associated with the romantic Spanish period—a fairyland of natural and cultivated beauty.

To the north there are many cities to claim your attention. Vancouver, in British Columbia, built up against mighty mountains with a primeval forest almost at its environs. Seattle, the great shipping center of the northwest, with Puget Sound to the west and beyond it the white-capped Olympics. In the distance the Cascade Mountains and looming to the southeast, Mt. Rainier, held in special veneration by the Indians as "the mountain that was God"—no peak in the United States is so majestic. Portland, famous for its natural beauty—a literal bower of roses. The blue miracle of Crater Lake, Mt. Shasta and Lassen Peak, the only active volcano in the United States.

Traveling through the mountains one will enjoy the grandeur of the high Sierras, and a visit en route to the Mormon capital—Salt Lake City—will be a notable feature of the journey.

No matter what route one takes he will view a truly great and inspiring American scene—the thriving farm lands of the midwest, the noble stretches of prairie, the sublime mountain ranges of the Rockies, the grandeur of the desert, the towering forests of the far west, and then the blue Pacific.

This year one will travel in comfort and luxury undreamed of a short time ago. Whatever route one travels he will find his train air-conditioned. This single factor adds so much to the comfort and pleasure of a transcontinental journey that it definitely and certainly marks the beginning of a new era in transportation history.

#### RAILWAY FARES FROM VARIOUS CITIES TO SAN FRANCISCO AND RETURN

Low round-trip fares will be in effect from all points in the United States and Canada. Consult your local ticket agent as to exact fare. Tickets are good going via one route and returning via the same or any other authorized route. Final return limit November 30.



	Round Trip Fare	Lower Berth One W'y
Atlanta	\$ 00 75	5
Baltimore	30 75	24 00
Boston	54 80	5 25
Buffalo	09 55	25
Chicago	26 00	5 75
Cincinnati	07 00	9 50
Cleveland	55	9 50
Detroit	08 30	9 50
Elizhth	26 00	7 75
Kansas City	7 00	3 5
Memphis	25 5	4 30
Minneapolis	26 00	5 75
Montreal	12 55	24 75
New York	26 00	24 75
New Orleans	25 5	4 00
Omaha	7 00	3 5
Philadelphia	25	24 00
Pittsburgh	07	20 5
St. Louis	22 50	5 00
St. Paul	26 00	5 75
Toronto	08 5	18
Washington	20 75	14 00
Winnipeg (via Portland)	26 00	5 75

#### HEADQUARTERS—TECHNICAL EXHIBITION

Headquarters for the Congress will be established at the Fairmont and Mark Hopkins hotels. At the former the Terrace Ballroom and Lounge, the Gold Ballroom and other large rooms on the main floor and on the terrace have been reserved for scientific sessions and conferences, registration and clinic ticket bureaus, bulletin boards, exhibits, executive offices etc. The Peacock Court and Room of the Dons at the Mark Hopkins will be utilized for various scientific sessions.

The Technical Exhibition, including the registration and clinic ticket bureaus, will be located in the ballroom and lounge on the terrace floor of the Fairmont Hotel. In these rooms will also be found the bulletin boards on which the daily clinical program will be posted each afternoon. The leading manufacturers of surgical instruments, X-ray apparatus, operating room lights, hospital apparatus and supplies, ligatures, dressings, pharmaceuticals and publishers of medical books will be represented in this exhibition.

#### ADVANCE REGISTRATION

The hospitals and medical schools of San Francisco and Oakland afford accommodations for a large number of visiting surgeons, but to insure

against overcrowding, attendance at the Congress will be limited to a number that can be comfortably accommodated at the clinics—the limit of attendance being based upon the result of a survey of the amphitheaters, operating rooms, and laboratories of the hospitals and medical schools to determine their capacity for visitors. It is expected, therefore, that those surgeons who wish to attend the Congress will register in advance.

Admittance to all clinics and demonstrations will be controlled by means of special clinic tickets, which plan provides an efficient means for the distribution of the visiting surgeons among the several clinics and insures against overcrowding, as the number of tickets issued for any clinic will be limited to the capacity of the room in which that clinic will be given.

A registration fee of \$5.00 is required of each surgeon attending the annual Clinical Congress, such fees providing the funds with which to meet the expenses of the meeting. To each surgeon registering in advance a formal receipt for the registration fee is issued, which receipt is to be exchanged for a general admission card upon his registration at headquarters. This card which is non-transferable, must be presented in order to secure clinic tickets and admission to the evening meetings.

#### SAN FRANCISCO HOTELS AND THEIR RATES

In addition to the two headquarters hotels—the Fairmont and Mark Hopkins—there are a number of first-class hotels within short walking distance of headquarters providing ample hotel facilities at reasonable rates. The following hotels are recommended by the Committee.

	Minimum Rate with Bath	
	Single	Double
Bellevue, Geary and T. Ylor	\$3 00	\$4 00
Californian, T. Ylor and O'Farrell	5 00	4 50
Citiz, Geary and T. Ylor	3 30	5 00
El Cortez, Geary near T. Ylor	2 00	4 30
Fairmont, Mason and California	2 30	5 00
Gaylord Jones near Geary	3 00	4 00
Mark Hopkins, Mason and California	2 50	5 00
Palace, Market and New Montgomery	2 50	5 00
Plaza, Post and Stockton	2 00	4 00
San Francisco Drake, Powell and Sutter	3 50	5 00
Stewart, 323 Geary	3 30	4 00
St. Francis, Union Square	3 30	5 00

# PRELIMINARY CLINICAL PROGRAM

GENERAL SURGERY, GYNECOLOGY, OBSTETRICS, ORTHOPEDICS, UROLOGY,  
SURGICAL PATHOLOGY, ETC

OPERATIVE CLINICS IN SAN FRANCISCO HOSPITALS—DAILY

## SAN FRANCISCO HOSPITAL

*University of California Service*

HAROLD BRUNN, GEORGE K. RHODES, A. R. KILGORE,  
C. L. CALLANDER, S. H. MENTZER, A. L. BROWN,  
H. W. STEPHENS, F. S. FOOTE, M. W. DEBENHAM,  
H. M. BLACKFIELD and L. GOLDMAN General surgery  
F. HINMAN, C. JOHNSON, S. OLSEN, L. PLAYER, J. J. SULLIVAN, W. A. CARROLL and T. O. POWELL. Urological operations  
W. G. MOORE, A. M. VOLLMER and M. SCHULZE. Gynecological operations  
H. W. FLEMING, H. A. BROWN and L. B. LAWRENCE. Neurosurgical operations.  
LEROY ABBOTT, F. G. LINDE, F. C. BOST, W. J. COX and K. O. HALDEMAN Orthopedic operations

*Stanford University Service*

LEO ELOESSER. Lobectomy for lung tumor, flap operation for tuberculous empyema, disarticulation at knee joint.  
W. L. ROGERS. Apicolysis (paraffin fill)  
J. M. MEHEREN. Gastric resection (Billroth I)  
EDMUND BUTLER. Pyloroplasty for peptic ulcer, atresia of colon, congenital.  
J. CLINE. Exploration of biliary duct.  
C. MATHEWSON. Open reduction of spiral fracture of the tibia, sequestrectomy for tuberculosis of the pelvis.  
D. KING. Nonunion of carpal scaphoid.  
M. R. OTTINGER. Resection for carcinoma of the colon  
E. TOWNE. Laminectomy for decompression of cauda equina  
E. MORRISSEY. Removal of cord tumor  
L. REYNOLDS. Cystectomy for carcinoma of the bladder  
G. HARTMAN. Suprapubic prostatectomy  
L. MICHAELSON. Plastic on kidney pelvis  
R. CRAIG. Nephrectomy  
K. SCHAUFF. Removal of fibromyoma of the uterus  
A. PETTIT. Vesicovaginal fistula  
H. VON GELDERN. Penneal repair operation  
C. COOLEY. Operation for pelvic inflammatory disease  
R. DUNN. Hyam's conization of the cervix  
D. DALLAS. Vaginal hysterectomy

## UNIVERSITY OF CALIFORNIA HOSPITAL

HOWARD C. NAFFZIGER, D. JONES, JR., H. BROWN and R. AIRD. Neurosurgical operations  
HAROLD BRUNN and H. STEPHENS. Thoracic surgery  
R. ABBOTT, F. BOST, K. HALDEMAN and W. KEYS. Orthopedic surgery  
FRANK W. LYNCH, A. MAXWELL, M. SCHULTZE, D. MORTON and C. HAYDEN. Gynecological and obstetrical operations  
FRANK HINMAN, C. JOHNSON, S. OLSEN and B. WAYMAN. Urological operations.  
W. S. TERRY. General surgical operations, thyroidectomy  
H. SEARLS and H. GLENN BELL. Carcinoma of colon, cholecystectomy, popliteal aneurism  
C. ROSSEN. Appendectomy, hernioplasty  
M. S. WOLFE. Carcinoma of rectum and lower bowel.  
F. FOOTE. Partial obstruction, new operations.  
E. O. BARTLETT. Carcinoma of breast.

## STANFORD UNIVERSITY HOSPITAL

EMMET RINFORD, EDMUND BUTLER, R. GILMAN, L. CHANDLER, EMILE HOLMAN and S. BUNNELL. General abdominal surgery, gastro intestinal surgery, hernias  
EMILE HOLMAN and LEO ELOESSER. Thoracic surgery  
F. REICHERT and E. TOWNE. Neurosurgical operations  
R. GILMAN, EMMET RINFORD and EMILE HOLMAN. Thyroid, biliary tract, liver and pancreas surgery  
A. L. FISHER, D. KING and M. MENSOR. Orthopedic operations  
J. DILLON and L. REYNOLDS. Urological operations  
L. ENGEL, H. A. STEPHENSON, C. FLEUHMANN, P. E. HOFFMAN, G. CRAIG and W. STEVENS. Gynecological and obstetrical operations  
F. REICHERT and EMILE HOLMAN. Cardiac conditions, circulatory diseases  
C. B. PALMER and R. BURROWS. Injections, anesthesia.  
R. A. SCARBOROUGH. Proctological operations  
A. DAVIS and S. BUNNELL. Plastic surgery, industrial cases, skin diseases

## MOUNT ZION HOSPITAL

HAROLD BRUNN. Total thyroidectomy for cardiac disease.  
F. I. HARRIS. Torek operation for undescended testicle, first and second stage procedures, resection for lesions of descending colon, radical mastectomy, Percy cautery and endotherm  
A. L. BROWN. Plastic repair of pendulous breasts, herniotomy  
W. WALDEYER. Appendectomy  
M. GROPER and A. WHITE. Blood transfusion, citrate, Linderman and Unger methods  
L. HOFFMAN. Hysterectomy  
L. D. PRINCE, A. SIRBU and DAVID CHARMAN. Radical clavectomy, fracture of os calcis  
H. BLACKFIELD. Plastic correction of congenitally protruding ears  
HAROLD BRUNN and A. L. BROWN. Phrenic avulsion, thoracoplasty  
A. ZOBEL and D. A. SUSNOW. Electrocoagulation of tumors of the rectum, hemorrhoidectomy under local infiltration  
L. C. JACOBS. Calculi of the urinary bladder, transurethral prostatectomy  
H. A. R. KREUTZMANN. The problem of urinary lithiasis, nephrotomy, pyelotomy, nephrectomy  
B. STRAUSS and M. POLSE. Hydrocele operation, plastic operation for phimosis, cystoscopy  
A. EPSTEIN. Injection of vas deferens for chronic epididymitis  
R. K. SMITH. Classical cesarean section  
A. BERNSTEIN. Demonstration of cervical repair immediately following delivery  
F. PEARL. Muscle splitting extraperitoneal lumbar sympathetic ganglionectomy, a new approach, muscle splitting posterior cervicodorsal sympathetic ganglionectomy  
EDWARD H. BOLZE, HERBERT H. SCHULTZ and DR. LAZAR. Demonstration of introduction of anesthesia by avertin, evipal, gas and oxygen, spinal.

## SOUTHERN PACIFIC HOSPITAL

- W B CONROY and J D HENNER. Superior cervical sympathectomy for angina pectoris, moving picture demonstration in natural color  
 C MAHES and T GIBSON. Transurethral prostatectomy  
 E GREENWOOD. Cholecystectomy  
 F R GERARD. Inguinal hernia: ambulant treatment by injection  
 C WALKER and J BOWEN. Open reduction of fractures  
 OSCAR F MOLAN and THOMAS E GIBSON. Suprapubic prostatectomy  
 W W WASHINGTON. Thyroid surgery

## ST LUKE'S HOSPITAL

- ALANSON WHEELER, G D DELPRAIT PAUL CASTELNUK, A H ROBERTS, OTTO H FLEISCHER, DR SOTELVAY, D MOORE and ALBERT M VOLLMER. General surgical operations.  
 GEORGE J MCCARTNEY, RUDOLPH L DARRER and D COY. Orthopedic operations  
 L F FLAYER, HERBERT D CHALL and MILLY B WILSON. Urological operations  
 J M MORRIS. Proctological operations

## U S MARINE HOSPITAL

- ROBERT A JONES. Excision of pilonidal sinus and rectal operation, cholecystectomy and autoplasty (Guthrie tubular flap) Dupuytren's contracture  
 ROBERT L W ROSE. Inguinal hernioplasty using pedicled fascial strips, operation for scabies (Heyden) arthroscopy of the knee with excision of internal semilunar cartilage, bunion operation (Pembrey) splenic aneurysmectomy  
 FLETCHER C STEWART. Transurethral resection of prostate

## ST FRANCIS HOSPITAL

- G B O'CONNOR. Plastic surgery. Reconstruction of face after burns, rib cartilage transplant to the nose, removal of nasal hump, cleft palate reconstruction surgery of the hand  
 W W WASHINGTON. Thyroidectomy  
 L R REYNOLDS and O NOLA. Prostatectomy, arterial transplants

## SHRINER'S HOSPITAL

- SYL AN L HAAS. Longitudinal osteotomy, transplantation of muscles in paralysis, stabilization of foot, fusion of spine, lengthening of leg, congenital dislocation of hip, Sever operation for obstetrical paralysis, rib transplantation of tibiae, major fusion of hip, plastic operation

## FRANKLIN HOSPITAL

- E GERRARD. Gastro-intestinal surgery  
 L BROOKS. Abdominal operations  
 J SALL, V DELLO, W MCWINDY and W COX. Intra-abdominal surgery and orthopedics  
 G W PEARCE and O O'CONNOR. Reconstruction surgery of hand, face and neck after burns, spasm of eyelids, correction of flexion contractures

## ST MARY'S HOSPITAL

- T E BAILEY. Gastric surgery, gastrectomy  
 ROBERT YONKEL. Gall bladder surgery, cholecystectomy  
 D SOOT. Surgical intervention for diaphragmatic hernia  
 C P M DEE. Nephrectomy for nephroptosis  
 E TORRAN. Inguinal hernia  
 JUSTIN MCCARTNEY. Intra-abdominal emergency cases  
 EDWARD BUTLER. Surgery of the colon  
 GEORGE K. RICHES. Emergency surgery  
 EDWARD MCLENNAN. Sympathectomy for Raynaud's disease  
 PHILIP ARNOT. Obstetrical surgery  
 T GIBSON. Nephrectomy  
 W FAULKNER. Bronchoscopic diagnosis of lung abscess  
 J LOUGHEED. Out treatment for delayed bony union.

## LETTERMAN GENERAL HOSPITAL

- R F MITCHELL. Castration of cervix; pericardiectomy; suspension of uterus; gastrojejunostomy; cholecystectomy; hemorrhoidectomy; colostomy for rectal carcinoma; caesarean section  
 P L COOK. Hernia, appendectomy, inguinal hernia, vesical hernia  
 H S BLISSER. Genito-urinary operations, electrical resection  
 B S BURNEY. Thoracotomy for empyema, orthopedic operations, bone graft, open reduction of tibia, excision of cartilage, knee  
 P E DUDGON. Carriage and insertion of Carver pessary for sterility

## ST JOSEPH'S HOSPITAL

- ALBION R. KILGORE, J M MCNEELY, F SEELY and C E SMITH. General surgical operations  
 R SOTO-HALL and K BALDWIN. Orthopedic operations  
 E MCNEELY. Neurosurgical operations  
 H VAN GELDEREN. Gynecological operations  
 T GIBSON. Urological operations

## FRENCH HOSPITAL

- F A LOWE. Fractured humerus, internal derangements of knee joint  
 G W PIERCE and G O'CONNOR. Removal of nasal hump

## MARY'S HELP HOSPITAL

- R MILLER. Radical neck dissection  
 E CARLSON and C C MCCRAE. Abdominal operations  
 M MESSER and L PARKER. Orthopedic surgery  
 M VICKI. Urological operations  
 H VAN GELDEREN and A SCHINDL. Gynecological and obstetrical operations

## HOSPITAL FOR CHILDREN

- C HOAG. Thyroidectomy  
 MICHELLE FOX and THYNGLOM diet cyst.  
 ALAN PETERSON. Supra-umbilical hysterectomy, total hysterectomy, vaginal plastic

## VETERANS ADMINISTRATION

- Staff. Colley operation for carcinoma of the rectosigmoid, second stage gastrectomy

## CLINICAL DEMONSTRATIONS IN SAN FRANCISCO HOSPITALS—DAILY

## GENERAL SURGERY

- A S WHITE and F I HARRIS Injection treatment of hernia
- HAROLD BRUNN Appendicitis
- S R SHERMAN Rupture of the spleen
- J HOMER WOOLSEY and H GLENN BELL Splenectomy
- WALTER B COFFEY Inspection of an industrial medical and surgical center, ward rounds, demonstration of cases, postoperative treatment
- EMMET RIXFORD Knotty problems in industrial surgery
- Traumatic carcinoma of breast, ruptured heart, traumatic thrombosis of iliac and other large veins
- EMILE HOLMAN Operative cure of recurrent and direct inguinal hernia
- GEORGE K. RHODES Hematogenous perinephric abscess, peritonitis and drainage
- M W DEBENHAM Aseptic meningitis following spinal anesthesia
- A L BROWN Pulmonary embolectomy, motion picture demonstration of the Trendelenburg operation on cadaver
- H. BRODIE STEPHENS Subphrenic abscess, vaccination of the pleural and abdominal cavities
- WALTER BIRNBAUM Tendon repair, acute gonococcal tenosynovitis
- ALSON R. KILGORE, OTTO H. PFUEGER and R S STONE Treatment of breast cancer, end results
- OTTO H. PFUEGER Soft tissue sarcomas
- ALSON R. KILGORE Cystic disease of the breast, cancer
- C L CALLANDER Gas bacillus infection, new amputation of thigh in lower third, treatment of septic joints
- EDMUND BUTLER Emergency surgery
- EDMUND BUTLER, L R. REYNOLDS, L H GARLAND and J B McNAUGHT Old healed ruptured bladders, diagnostic difficulties and value of X ray in diagnosis, X ray in differential diagnosis of acute abdomen
- EUGENE S KILGORE Circulatory disease in differential diagnosis of acute abdomen
- CARLETON MATHEWSON, JR and J B McNAUGHT Lymphogranuloma inguinale
- A S MUSANTE Postoperative infections
- I. W. THORNE Squamous and basal cell carcinoma of face and neck, pathology, diagnosis and treatment.
- Z E BOTIN Biopsies and tumor surgery, mixed tumors of the parotid
- EVERETT CARLSON Carotid body tumors, splenectomy, indications and technique.
- FRANK E STILES Treatment of varicose veins
- J F RICKARD Intestinal obstruction

## SURGERY OF THE THYROID

- WILLIAM J KERR, HENRY H. SEARLS, JANE T PAXSON and R S STONE. Activities of the thyroid committee of the University of California Hospital with follow up studies after various lines of treatment
- HENRY H. SEARLS, E I BARTLETT and C L CONNOR. Chronic diffuse thyroiditis
- HENRY H SEARLS and JANE T PAXSON Clinical picture of toxic adenoma with normal or lowered metabolic rate.
- WILLIAM J KERR. The heart in hyperthyroidism
- M L MONTGOMERY Lingual thyroid
- THEODORE ALTHAUSEN Surgical implications of hepatic damage in thyrotoxicosis
- R J MILLNER Parathyroid damage during thyroidectomy

## GENITO-URINARY SURGERY

- FRANK HYMAN, CLARK M JOHNSON and BRENT WEYMAN Tumors of the testicle, pathology, demonstration of hormone tests, end results, uretero-intestinal anastomosis, experimental work, drawings and motion picture demonstration, demonstration of patients, prostatism, pathology, indications for different types of surgery, end results by different methods
- C P MATHE Surgery of the prostate
- T E GIBSON Newer aspects of renal tuberculosis
- L P PLAYER and H D CRALL Gracilis transplantation for urinary incontinence
- MILEY B WESSON Conservative surgical treatment of nephrolithiasis
- L C JACOBS Calculi of urinary bladder, suprapubic and transurethral prostatectomy
- H A R KREL TZMAN Urinary lithiasis, nephrotomy, pyelotomy and nephrectomy
- BERNARD STRAUSS and M L POLSE Operation for hydrocele, plastic operation for phimosis
- A EPSTEEN Injection of vas deferens for chronic epididymitis
- J V LEONARD and GEORGE W HARTMAN Demonstration in urology
- C P MATHE and T E GIBSON Transurethral prostatectomy
- T E GIBSON and O F NOLAN Suprapubic prostatectomy
- J R DRILLON Treatment of chronic pyelitis and pyelonephritis, treatment of cancer of prostate, technical improvements in surgical treatment of undescended testicle
- W E STEVENS Unusual pathological conditions of the urinary tract in women.
- EDGAR POTH A new aseptic technique for uretero-enterostomy, mechanism of ascending infection of the urinary tract, experimental observations
- SYDNEY OLSEN Tuberculosis of the genito-urinary tract, urinary calculi
- CLARK M JOHNSON Trauma of the genito-urinary tract, infections of the genito-urinary tract, renal and para renal infections, renal anomalies.
- L P PLAYER. Kidney lavage.
- W A CARROLL. Ureteral lithiasis, rupture of kidney
- T O POWELL. Newer knowledge of tumors of the testicle with special reference to gonadotropic hormone excreted in the urine.
- M R. OTTINGER, LLOYD R. REYNOLDS and J B McNAUGHT Torek operation for undescended testicle, torsion of testicle
- GEORGE W HARTMAN Hematuria and pyuria, renal tuberculosis
- W A SUMNER. Relationship of chronic infections to lesions of the genito-urinary tract.
- LEWIS MICHELSON Obstruction of the neck of the bladder in the female.
- R GLENN CRAIG Ureteral pain of obscure origin
- MORRELL VECKI Renal mobility
- ENDOCRINOLOGY
- R F ESCAMILLA Consideration of abdominal pain of endocrine origin
- SAMUEL COHN and F I HARRIS Discussion of the treatment of undescended testicle by operation and glandular extracts
- LEO STANLEY Endocrinology in a penal institution.

## SURGERY OF THE GASTRO-INTESTINAL TRACT

- HAROLD BRUNY. Cancer of the rectum.
- F I HARRIS. Causticizing (chronic) enteritis (regional ileitis) treatment of appendix stump, neoleostomy.
- FRED H KATZ. The more common complications of peptic ulcer.
- E J BRYT F H KATZ, THEODORE ALTHAUSSEN and RALPH RANDOWITZ. Postoperative care of intestinal conditions.
- M F COHEN. Primary duodenitis, end results of ulcer cases, types of operation, causes of recurrence.
- LEON GOLDMAN and THEODORE ALTHAUSSEN. Pseudo perforation of peptic ulcer.
- J HOMER WOOLLEY and H GLENN BELL. Carcinoma of stomach.
- M L MONTGOMERY and JOSEPH M SWITZER. Acute intestinal obstruction, experimental and clinical.
- H GLENN BELL. Subacute intestinal obstruction, localized type (chronic causticizing enteritis).
- H GLENN BELL and LEON GOLDMAN. Congenital lesions, tumors, diverticula of small bowel.
- M B WOOLLEY, LEON GOLDMAN and H GLENN BELL. Carcinoma of large bowel.
- DUDLEY SMITH and J W MORGAN. Carcinoma of rectum.
- ARA W COLLINS. Pylorotomy and gastro-enterostomy.
- LEROY BROOKS. Diagnosis and treatment of intestinal obstruction.
- F K BROWN. Peptic ulcer indications for surgical treatment.
- W W WASSERMAN. Acute perforation of peptic ulcer complications and end results in 50 cases.
- LEONARD COHEN. Radical surgery for gastric and duodenal ulcers, diverticulitis of colon, closure of colostomy preservation of anal sphincter.
- J A GILLFILL. Chronic appendicitis, end results of operation.
- J E BONE. Mortality rate of operations for appendicitis.
- R A SCARBOROUGH. Developments in surgical treatment of carcinoma of rectum, 300 cases.
- EMILE HOLMA. Causes for failure to control symptoms and to prevent gastrojejunal ulcer in gastric surgery.
- GEORGE W NAGEL, F L REICHERT and MARY E MATTHEW. Chronic regional enteritis, clinical, experimental.
- D VID A. WOOD. Multiple primary carcinomata of colon complicating multiple polyposis of colon.
- NELSON J HOWARD. Anemic granulomas of large bowel.
- HAROLD BRUNY. Carcinoma of large bowel carcinoma of rectum, bowel obstruction.
- GEORGE K REICHERT. Spontaneous perforation of cecum from obstruction in distal colon.
- DANIEL BOY. Choice of operation in gastric surgery.
- LOW REID TOPHAM. End results in surgery for gastric ulcer.
- H P HILL, GEORGE RANDITT, J M MERRITT, J W CHICK, J CARLETON MATTHEWSON, J J B Mc NAUGHT and A C McKENNEY. Lesions of the upper gastro-intestinal tract, anaerobic infections of liver and gastro-intestinal tract.
- DUDLEY SMITH. Operation for rectal fistula and hemorrhoidectomy motion picture demonstration.

## SURGERY OF INFECTIONS

- A S WHITE. Treatment of staphylococcus infections with staplashol.
- S A GOLDMAN. Studies on staphylococcus infections.
- F J MCCARTHY. End results in infections of the hand.
- B F ALDER. Relation of focal infection to Wassermann-fast test.
- V H MITCHELL. Treatment of anaerobic infection of the extremities, presentation of cured patients.

## THORACIC SURGERY

- HAROLD BRUNY, A L BROWN, H ROSEWALD and J J SANDFORD. Symposium on surgery of the heart with particular reference to adhesive pericarditis.
- LEO ELLERRE, PHILIP H PIERSON, W L ROOTES, W G BURGLAND, D VID A WOOD, W R CLARK and L H GARLAND. Various types of bronchial stenosis mycotic infections of the lung, tumors of the lung; emphysema.
- EMILE HOLMA. Technical improvements in partial selective thoracoplasty resection of transverse process, resection of scapula, ligation of the pulmonary artery as therapeutic measure in pulmonary hemorrhage carcinoma of lung associated with infectious disease.
- HAROLD BRUNY, SCOTNEY J SMITH, H BROOKS STEPHENS, A L BROWN, M W DIERMEYER and A GOLDMAN. Lung suppuration, emphysema; artificial pneumothorax, pleuric fistula thoracoplasty.
- ALANSON WEEKE and G D DELPRAY. Thoracoplasty.
- RA KUTLER. Diaphragmatic hernia.
- SCOTNEY J SMITH. Pneumothorax in pneumococci.
- W B F OLIVER, J BROCKHOUTS, treatment of chest injuries.
- A L BROWN. Collapse therapy in pulmonary tuberculosis.
- S STEINMAN. Lymphomatous of mediastinum.
- C A WALLER. Thoracotomy for pericardial adhesions.
- A GOLDMAN. Staphylococcal infections of the lung, chemotherapy in tuberculosis.
- T F MULLER. Antiseptic thoracoplasty.
- MARY E MATTHEW. Experimental study of the effect of various pathological conditions upon the dual blood supply of the lungs.
- EMILE HOLMA. A simple apparatus for tidal and apnoea irrigation and its application in treatment of emphysema.
- D VID A WOOD and MARY E MATTHEW. Exhibit of clinical and experimental observations on the dual blood supply of the lungs in various pathological states.

## SURGERY OF THE BILIARY TRACT LIVER AND PANCREAS

- ALANSON WEEKE and G D DELPRAY. Common duct stone, hydatid disease of liver, granular hepatoma.
- F I HARRIS. Acute cholecystitis.
- CARL HOWE. Reconstruction of common duct.
- H CLARK SHEPARDSON and HANS LIEBER. Pancreatic dysfunction, hypoglycemia.
- H GLENN BELL and THEODORE ALTHAUSSEN. Operative mortality and pre-operative management of cholecystitis, cholecystectomy, Rose-Bengal and other tests.
- FRED H KATZ and THEODORE ALTHAUSSEN. Medical and surgical pancreas curables of liver differential diagnosis from carcinoma of stomach.
- JAMES L CAKE and FREDERICK S FOOTE. Experimental work in human pancreas.
- KARL SCHMIDT. The bile salts.
- EMILE HOLMA. Postoperative and inflammatory stenosis of the bile passages.
- M W DIERMEYER and J M SWITZER. Liver abscess.
- STANLEY H MERRITT. Acute cholecystitis, obstructive cholecystitis.
- ROBERT A YORLL. Gall bladder anomalies.
- T F MULLER. Recurrence of symptoms after biliary tract surgery.

## CIRCULATORY DISEASE

- M L MONTGOMERY. Therapeutic venous occlusion.
- C A NOBLE, JR. Postoperative cardiac venous circulatory collapse.

## ORTHOPEDIC SURGERY

- GEORGE J MCCHESNEY, W COX and R L DRESEL  
Fracture of neck of femur, treatment without external splinting
- L D PRINCE, A B SIRBU and D D CHARMACK  
Fractures of os calcis, replacement of tibial shaft by fibula following osteomyelitis, treatment of bursitis
- R L WAUGH  
Clinical demonstration of Roger Anderson "Ought-O-Matic" splint and skeletal traction and countertraction methods applicable to Thomas or Hodgen splints
- LEROY C ABBOTT  
The shoulder joint.
- JOHN B DE C M SAUNDERS  
The shoulder joint.
- J F RINEHART  
Vitamin C deficiency in arthritis
- KEENE HALDEMAN and JOHN B DE C M SAUNDERS  
Demonstrations of bone growth
- FRANCES BAKER  
Heat therapy
- A A LOWE  
Internal derangements of knee joint, clinic and motion picture demonstration, fracture of humerus, clinic and motion picture demonstration
- J J LOUTZENHEISER  
Arthrodesis of foot.
- S L HAAS  
Application of Hibbs-Risser plaster for scoliosis, results of treatment for scoliosis, results of tendon transplantation, Leggs-Perthes disease
- J J SALE, W O MONTGOMERY, V M DILLON and W J COX  
Industrial surgery and orthopedics
- J H O'CONNOR  
Reduction of complicated fractures, closed methods, demonstration of cases, indications for open reduction
- C A WALKER  
End-results of open reduction of fractures, treatment of compression fractures of spine, 250 cases, fractures of clavicle and patella.
- W W WASHBURN  
Disabilities following fractures, factors influencing period of recovery
- LEONARD W ELY  
Arthritis of the hip
- D KING  
Functional anatomy and pathology of the shoulder joint.
- A L FISHER  
Treatment of flat feet.
- MERRILL C MENSOR  
Osteogenic sarcoma of spine, relation of bacteriophage to the Orr treatment of osteomyelitis
- NELSON J HOWARD  
Traumatic lesions of bursae, tendons and muscles
- LEON PARKER  
Familial tendencies in Paget's disease
- D KING  
Treatment of chronic sclerosing osteomyelitis
- F G LINDE  
Compression fractures of spine, non union of fractures
- F C BOST  
Hibbs-Risser treatment of scoliosis, dislocation of carpal semilunar, fracture of ankle, ligamentous tears of ankle, treatment of fracture of os calcis
- W J COX  
Internal derangement of knee joint, rupture of ligaments, treatment of fracture of femoral neck with Smith Peterson nails
- KEENE O HALDEMAN  
Pathology of acute osteomyelitis, pathology of chronic infections of bone
- RALPH SOTO-HALL and KEENE O HALDEMAN  
Fracture dislocation of cervical spine, Duncan's traction apparatus.
- PAUL E JOHNSON, B H HENNING and JOHN A KENNEDY  
Disability ratings of Veterans Administration for orthopedic conditions of the extremities
- CARLETON MATHEWSON, JR. and J B MCNAUGHT  
Treatment of spiral fractures of tibia, open and closed methods of treatment of fractures of extremities, tuberculosis of pelvis
- D KING, J M MEHERIN and R A SCARBOROUGH  
Fracture of the carpal scaphoid, surgical approaches to bones and joints, the Orr method of treatment of osteomyelitis.

- NELSON J HOWARD  
Fractures of the upper end of the humerus, motion picture demonstration.
- MERRILL C MENSOR and LEON PARKER  
Unusual fractures of the spine, treatment of osteomyelitis with surgical maggots
- C C MCRAE  
Injuries of small bones of the hand
- EDGAR L GILCREEST  
Problems in treatment of fractures.

## GYNECOLOGY AND OBSTETRICS

- WILLIAM G MOORE  
Endometriosis, fibromyomata of uterus
- A M VOLLMER  
Rubin's insufflation test, trichomonas vaginals
- R. K SMITH  
Classical cesarean section, motion picture demonstration
- FRANK LYNCH, ALICE MAXWELL and R S STONE  
Uterine cancer, follow-up, X-ray therapy, radium therapy
- MARGARET SCHULZE  
Special ovarian tumors
- A H HEALD and ALICE MAXWELL  
X-ray pelvimetry, direct method.
- PHILIP H. ARNOT  
Conduct of labor in posterior position
- LUDWIG EMGE  
Dysmenorrhea, causes and treatment, sterility, diagnosis and treatment.
- C F FLUHMAN, P E HOFFMAN and GERTRUDE I JONES  
Endocrinological aspects of gynecology, modern methods of diagnosis, blood and urine hormone tests, biopsy of endometrium, hormone therapy
- A V PETTIT  
Results of hyperpyrexia in treatment of acute and chronic pelvic inflammatory disease
- LUDWIG EMGE  
Radiation therapy of carcinoma of cervix, methods and end results
- A. M VOLLMER  
Treatment of abortions
- MARGARET SCHULZE  
Multiple pregnancies, pyelitis with pregnancy, hydridiform mole and chorio-epithelioma, cardiac disease with pregnancy
- KARL L SCHAUFF  
Fibromyoma of the uterus
- HANS VON GELDERN  
Plastic operations on pelvis
- C L COOLEY  
Demonstration of gynecological cases
- R D DUNN  
Treatment of incomplete abortions.
- D A DALLAS  
Operations in obstetrics.
- BEVERLY SIMPSON  
Separated placenta.
- ADOLPH E SCHMIDT  
Uterine bleeding

## NEUROSURGERY

- HOWARD C NAFFZIGER  
Late results in the treatment of malignant exophthalmos, brain tumors, factors in influencing recovery after peripheral nerve injury, cervical ribs and "the scalenus syndrome without cervical ribs"
- HOWARD W FLEMING  
Subdural hematomata, cerebrospinal rhinorrhea, relief of intractable pain, cranial approach for orbital tumors, craniocerebral injuries
- EDMUND MORRISSEY  
Neurologic clinic on lesions of the cauda equina, diagnosis and treatment of subdural hemorrhage, diagnosis of subdural hemorrhage
- O W JONES, JR.  
Spinal cord tumors.
- H. A BROWN  
Low back injuries, spinal cord injuries
- E B TOWNE  
Treatment of acute head injuries
- F L REICHERT  
Neuralgias of cranial nerves, demonstration of patient and lantern slides
- ROBERT ATRD  
Cephalography, clinical and experimental, intradural alcohol injections for intractable pain
- E B TOWNE, E MORRISSEY, J W WOLFSOHN and D WOOD  
Surgical lesions of the spinal cord, dynamics of epilepsy
- L B LAWRENCE  
Spinal cord tumors, tumors of cauda equina
- LEE HAND  
Regeneration of peripheral nerves of hand.

## CLINICS IN ALAMEDA COUNTY HOSPITALS—WEDNESDAY

## ALAMEDA COUNTY HOSPITAL

- WHITFIELD CRAVE and W. EARL MITCHELL—9. Care of areas of stomach  
 FRANK H. BOWLES and THEODORE LAWSON—1. Cancer of rectum  
 H. W. HARRING and DON D. WEAVER—1. Cancer of colon  
 LEONUEL P. ADAMS—1. Cancer of breast  
 SUMNER EVEREDHAM—9. Extrapleural thoracoplasty in intrapleural pneumothorax, clinic on pleural interruption and thoracoplasty. Discussion by CLEVELAND ROSE  
 W. ERIC B. ALLAN—9. Neurosurgery  
 W. F. HOLCOMB—9. Arthroplasty of hip  
 L. B. HARRARD—9. Arthroplasty of shoulder  
 E. N. EWING—9. Total hysterectomy subtotal hysterectomy. Discussion of obstetrical service at Alameda County Hospital  
 CLARENCE A. DEPUY—1. Gynecological cancer clinic. Demonstration of intrapelvic alcohol injection and presentation of cases  
 ALBERT M. MEADE, LLOYD KENDALL, JOHN A. D. DOWNEY, T. I. BUCKLEY and associates—9. Perineal proctectomy suprapubic proctostomy. Perineoscopic proctostomy. Operations, demonstration of cases and discussion

## Dry Clinic, 8-10

- CHARLES A. DUCK and associates. Cancer clinic.  
 HAROLD H. HERRICK, N. A. CART and associates. Traumatic and orthopedic clinic, demonstration of Swarthland cast dryer, Bell table, plaster models, splints, etc.  
 W. H. SANBORN and C. B. BOYCE. X-ray exhibit and discussion  
 GEORGE MOORE. Pathological exhibit and conference

## BERKELEY CENTRAL HOSPITAL

## Dry Clinic, 9-11

- FRANK D. WALSH. Cholecystitis, observations and comments on surgical treatment  
 CLAUDE H. CRUICK. Ectopic pregnancy reacting on main side  
 WILLIAM W. CROSS. Polycystic kidney nephrotheliasis, proteolytic management  
 J. F. CARLSON. Osteochondromatosis involving all epiphyses in one extremity. Clinical diagnosis  
 W. W. REICH. Parathyroid disease, gross specimens and microphotographs  
 R. G. VAN NURS. X-ray demonstration and discussion

## CHILDREN'S HOSPITAL

- ROY NELSON—9. Demonstration of methods of treatment of esophageal stricture due to lye  
 W. W. CROSS—9. Postmortem findings in the kidneys of children, bacteriologic demonstration  
 CLIFFORD SWERT—9. Clinic on undescended testes. Demonstration of postoperative results, discussion of the effect of salivary S. demonstration of operation

## ALTA BATES HOSPITAL

- Staff—9. Operations and dry clinic

## SAMUEL MERRITT HOSPITAL

- WARREN B. ALLEN—9. Reconstruction of skull defects, operation and demonstration of cases  
 W. F. HOLCOMB and D. D. TONKES—9. Orthopedic operations and demonstrations  
 MARY L. FREDSON—9. Rectal surgery and presentation of cases  
 FRANK H. BOWLES—9. Thyroidectomy  
 W. H. SANBORN—9. X-ray demonstration and discussion of cases  
 ROBERT A. OLNEY—9. Pathological exhibit, demonstration of frozen section technique and specimens  
 WHITFIELD CRAVE—10. Typhic ulcer. Jocky pyeloplasty  
 W. EARL MITCHELL—10. Pelvic tumor  
 HERBERT KOPPEL—1. Cholecystectomy  
 CHARLES A. DUCK—1. Apicalydia, operation demonstration of thoracic cases. Discussion by HAROLD TENDLER  
 H. N. ROWELL, A. M. SMITH, W. H. STEINMANN, A. A. ALEXANDER, W. F. KOPPEL, STEWART V. JAMES, H. GORDON MACLE, FLETCHER B. T. TIGHE, VERA G. ALDERSON and HOWARD ROBERTS—1. Symposium on pre- and postoperative care. Management of surgical jaundice and stomach cancer. Diabetes in surgery, traumatic and postoperative pneumonia, cardiac and renal complications, postoperative psychosis. Allergy as relation to abdominal surgery. Discussion and demonstration of cases

## PIRALTA HOSPITAL

- J. I. LOOPER—9. Cholecystectomy  
 ERIC A. MAJORS—9. Cancer of breast, radical removal  
 F. M. LOOPER and JOHN W. SHERIDAN—9. Porto cavalic section  
 CHARLES B. FOWLER—9. Orthopedic treatment of epiphyseal lesions, correction of upper extremity involvement in poliomyelitis  
 H. J. TIMMONS and J. LOOPER—9. Elective desiccation in cutaneous malignancies  
 JOHN W. SHERIDAN—9. Vaginal plastic  
 T. H. BELL—9. Pelvic tumor  
 T. C. LAWSON—9. Hernia, laceral repair  
 P. N. JACOBSON—9. Bladder surgery  
 P. H. MERRITT—9. 10. Pathological demonstration and exhibit  
 J. D. COYNE—9. 10. X-ray demonstration and exhibit

## COWELL MEMORIAL HOSPITAL

- HERBERT E. AVER, ROBERT LOOPER, C. A. KOPPEL and associates—9. Exhibit and discussion of latest advances in endocrinology, inspection of laboratories and hospital with special reference to the systematic medical care of university students, discussion of laboratory techniques with particular reference to diabetes

## ALAMEDA SANATORIUM

- J. OAKS—9. Hernioplasty under local anesthesia  
 G. R. BOWEN—9. Cholecystectomy  
 CHAS. HALL—9. Resection of stomach

## PROVIDENCE HOSPITAL

- O D HAMLIN—9 Intestinal anastomosis  
 J RADFORD FEARN—9 Vaginal hysterectomy under local anesthesia.  
 A REIS—10. Cholecystectomy, new method  
 THEODORE M WELER—10 Cesarean section  
 N AUSTIN CARY—11 Sacro iliac fusion  
 PHILIP J DICK—11 Posterior gastro-enterostomy  
 MICHAEL TORRANO—12 Herniotomy under local anesthesia  
 S A JELTE—9 to 12 X-ray demonstration and discussion

## EAST OAKLAND HOSPITAL

- DON D WEAVER—9 Ulcer of the stomach  
 O R ETTER—9 Surgery in the diabetic patient, dry clinic.  
 R G VAN NUYS—10 Dry clinic Visceroproptosis and position of the viscera in healthy young adults, X-ray demonstration  
 BROOKS STEPHENS—10 30 Hallux valgus  
 CLAIR RASOR—10 30. Prolapse of uterus  
 ALEXANDER H. GRIFFITH—11 Carcinoma of the recto-sigmoidal juncture, Lahey technique

## SURGERY OF THE EYE, EAR, NOSE, AND THROAT

## CLINICS IN SAN FRANCISCO HOSPITALS—DAILY

## UNIVERSITY OF CALIFORNIA HOSPITAL

## Tuesday

- JOSEPH L. MCCOOL, FREDERICK C. CORDES, JOSEPH W. CRAWFORD, C. ALLEN DICKEY and DAVID O. HARRINGTON—9 Ophthalmological operations.  
 R. C. MARTIN and FREDERICK C. CORDES—9 Toti Mosher operation  
 WALLACE SMITH, LOUIS MORRISON and EDITH STOKER—9 Otolaryngological operations.

## Dry Clinics—2

- FREDERICK C. CORDES Surgery of traumatic cataracts.  
 J. W. CRAWFORD Tuberculosis of the eye  
 C. ALLEN DICKEY Surgery of the vertical muscles  
 DAVID HARRINGTON Contact glasses, practical demonstration  
 R. C. MARTIN and STERLING BUNNELL Injuries and repair of the facial nerve

## Thursday

- JOSEPH L. MCCOOL, FREDERICK C. CORDES, JOSEPH W. CRAWFORD, C. ALLEN DICKEY and DAVID O. HARRINGTON—9 Ophthalmological operations.  
 R. C. MARTIN and FREDERICK C. CORDES—9 Toti Mosher operation  
 WALLACE SMITH, LOUIS MORRISON and EDITH STOKER—9 Otolaryngological operations.

## Dry Clinics—2

- JOHN SAUNDERS Regional anatomy of the mastoid and pathways of infection of the intracranium  
 HOWARD C. NAFFZIGER Brain abscess arising from middle ear and mastoid infections  
 WALLACE SMITH Phlebitis and thrombosis following middle ear and mastoid infections

## Friday—2

- FREDERICK C. CORDES Surgery of complicated cataracts  
 J. W. CRAWFORD The eye in diabetes  
 C. ALLEN DICKEY The value of orthoptic treatment  
 DAVID HARRINGTON Tobacco amblyopia and its treatment.

## ST MARY'S HOSPITAL

## Thursday—2

- FRANCIS CONLAN, STANLEY BURNS and FRANK HAND Treatment of posterior sinusitis. Blood dyscrasias in relation to the ear, nose and throat. Treatment of bilateral abductor paralysis  
 FRANK HAND Radical antrum

## HOSPITAL FOR CHILDREN

## Thursday—2

- GEORGE N. HOSFORD and AVERY M. HICKS Technique for the determination of the hydrogen ion concentration of tears. The significance of pH of tears in ocular symptoms and treatment. Indications for and results of orthoptic training. Relation of vertical imbalance of extra-ocular muscles to gastric symptoms, posture, temperament and aptitude for school work and occupation. Congenital muscle palsy. Motion picture demonstration of O'Connor technique for heterophoria and heterotropia

## Days to Be Announced

- GEORGE N. HOSFORD and AVERY M. HICKS—9 Extraction of congenital cataract, muscle operations, O'Connor cinch shortening for simple exotropia, simple esotropia, vertical deviations, muscle transplants for external rectus palsy, superior rectus for paralysis of the superior oblique (Jackson's technique), Motais' operation for congenital ptosis, Toti Mosher operation for occlusion of nasolacrimal duct (with Drs. Martin and Hosmer)

## SAN FRANCISCO HOSPITAL

## Tuesday—2

- WARREN D. HORNER. External iridectomy, history, uses, technique and advantages.  
 C. ALLEN DICKEY and J. W. CRAWFORD Safety procedures in cataract operations, akinesis, intra-orbital injections, lid sutures, pre-operative medication  
 WARREN D. HORNER, C. ALLEN DICKEY and J. W. CRAWFORD The use of synthetic epinephrine bitartrate in ocular therapeutics.  
 AUBREY RAWLINS Osteoma of the antrum, some curious foreign bodies in the lungs, cases of recovery from otitic meningitis, extensive osteomyelitis of the frontal bone.  
 HARRINGTON B. GRAHAM Foreign bodies in the lungs, stenosis of the esophagus, cancer of the larynx  
 HARRINGTON B. GRAHAM and J. M. WOLFSOHN Extensive abscess of the meninges.  
 RAE ASHLEY Treatment of tuberculosis of the larynx

## STANFORD UNIVERSITY SCHOOL OF MEDICINE

## Wednesday—2

- FRANK RODIN Congenital and hereditary eye defects.  
 AVERY HICKS Ocular torticollis.  
 DOERFMAN FISCHER Retinal detachment, methods and results.



## MOUNT ZION HOSPITAL.

**Tuesday**

URGENT } CON. EDWARD LEWITT and JON SKAFF—O  
Tonal operations, local and general anesthesia, dis  
section. Slender anastomosis.

Wednesday—

HERBERT J. COMY, EDWARD LIPWETT and JOE SKAFF  
Symposium on Malacodactyls  
GEORGE S. LACHMAN Treatment of corneal ulcers  
CHARLES WEISS Recently developed concepts in the  
immunology and bacteriology of ulcers of the ocular  
membranes.

G. Y. R. SZ Pathological demonstration of anovulatory conditions.

Therefore

Staff—2. Naval operations. Submarine reaction, electro-regulation of torpedoes, mine survey.

#### Days to Be Announced

FRANK H. REED and GEORGE S. LARSEN — Ophthalmological operations. Cataract, strabismus, plastic and excelsis.

## SOUTHERN PACIFIC HOSPITAL.

**Procedures**

WILBUR F. SWEET and JOE C. WILLIAMS      Chorus and  
demonstration of chess.

## LETTERMAN GENERAL HOSPITAL.

### Inventory

A. E. SCHLAIFER and HERBERT H. PRICE—o. Tonsillectomies, adenoidectomies, general anesthesia.  
HARVEY C. MAYNELL—o. p. Eye surgery, general anesthesia. Strabismus correction by O'Connor tendon crush and by lamellar recession.

*PS and nucleolus*

A. E. SCHLESINGER—9. Tetracyclines, local anesthetic  
anal operations, local anesthesia.

## Discussion

HARVEY C. MAXWELL—Eye operations, local anesthesia, cataract extraction, pterygium transplant, strabismus correction.

**Exhiber**

A. F. SCHLA SR., HERBERT H. PRYK and HARVEY C. MAYNELL.—9. Severe surgery local anesthesia; extramural radical frontal rhinoplasty; radical maxillary anastomosis; bronchostomy; tracheostomy.

## ST LUKES HOSPITAL

### Twelve and Thirteen

JOSEPH L. MCCOOL, C. ALLEN DICKER, A. E. FROSTON  
and CHARLES B. TIS—Ophthalmological chair

## VETERANS ADMINISTRATION

**Staff.** Bronchoscopic examinations.

## CLINICS IN ALAMEDA COUNTY HOSPITALS—WEDNESDAY

## PROVIDENCE HOSPITAL

4. J. HOLLAND - Reconstructive of nose  
 ROBERT O. COVING - Muscle shortening, cataract,  
 Liposuction operation  
 GEORGE McALLISTER and NELSON KEELEY - Ear nose  
 and throat surgery  
 RICHARD WEAVER - Plastic surgery  
 ROY KELLER - Laryngoscopy and bronchoscopy  
 BRUCE STEINBERG - a. Cataract operation  
 FRANK B. STEE - Ear, nose and throat operations  
 MILTON H. SILVER - Ear nose and throat operations  
 ALEXANDER GILBERT - Ear nose and throat oper-  
 ations  
 W. A. MAGRATH - Eye operations  
 V. D. F. WOLD - Eye surgery  
 F. C. KRA - Ear, nose and throat surgery

R. J. NOTTVO—Eyes operations.  
P. J. LUTHER—Ear, nose and throat surgery.  
F. A. SPOON—Ear, nose and throat surgery.  
SYDNEY J. PARKINSON—Treatment of acute and subacute paranasal sinus infections, lantern slides and roentgen picture demonstration.

## Dry Creek, 2-10 to 15 m

Staff: Discussion of operation procedures, demonstration of exam, last two and motion picture demonstration

## ALAMEDA SENATORIAL

B. M. ~~h...~~ ~ Caland

**CHILDREN'S HOSPITAL**

M. E. Lamm—strabismic, convergent treatment.

# SURGERY, GYNECOLOGY AND OBSTETRICS

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## PRIMARY MALIGNANT TUMORS OF THE OVARY

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From the State Institute for the Study of Malignant Diseases Buffalo New York Burton T. Simpson, M.D. Director

THIS paper is an attempt to clarify the relationship between the clinicopathological picture of primary malignant neoplasms of the ovary and the therapeutic end-results. It is based on a study of 92 patients who have been admitted to this Institute for diagnosis and treatment. Only those cases in which pathological material is now available for review have been selected.

The ovary, being an organ of both extrinsic and intrinsic function, plays an important rôle in the vital metabolism of the body. Its origin, development, and subsequent gross and histological transformations present a complex background in the interpretation of the various malignant growths which affect it. The divergent theories of origin and development of these neoplasms find their champions with proof of both plausible and fantastic accuracy.

Some observers believe that normal somatic cells may change gradually through a benign neoplasm into a malignant growth. Stevens denies this possibility of the supervention of cancer in an innocent neoplasm. Sampson has suggested that endometrial cysts may be precancerous lesions and presented evidence in 7 of 16 ovarian cancers examined. He described endometrium-like tissue in the site of the malignancy. Taylor could not find even the smallest indication of a practical or theoretical structural ground for a separation of an "endometrial carcinoma" from the germinal epi-

thelium carcinoma of the ovary. This germinal epithelium, which Maximow derives from mesothelium and Fischel claims arises from mesenchyme, gives rise to structures which may be both intra-ovarian and extra-ovarian. Certain of the structures remain after birth either in a functional capacity or as atrophied remnants in the ovary itself, the mesovarian, or in the broad ligament.

It does seem reasonable that cells or groups of cells normally found in the ovary may undergo malignant changes with all the possibilities of structural and morphological transformations seen in tumors of much simpler origin. The rare occurrence of extra-ovarian tissues in the ovary and the bizarre cellular growths resulting from embryonal rests and ovulogenic tumors is admitted. But these are the exceptions and not the rule in the origin of most ovarian neoplasms.

The tumors of this series are divided into three main groups, namely (1) adenocarcinoma, (2) carcinoma, and (3) embryoma.

The question of a tumor being cystic or solid has had no real bearing on this classification. As Taylor has pointed out, "true solid tumors are extremely rare and seem as a rule to be of teratomatous or sarcomatous nature."

The structure of the neoplasm and the morphology of stroma and epithelium have been the deciding factors. Suffice it to say that not all sections of the same growth are identical. One may see a change from cystic papillary

structure to almost diffuse epithelial tumor. Metaplasia of cells increases the difficulty of accurate identification. But the predominant and most constant cellular characteristics have determined our final decision.

The division into three main groups not only simplifies a most complex problem, but also provides a working basis in the interpretation of the therapeutic end results.

#### PATHOLOGY

1. Under *adenocarcinoma* are grouped those tumors showing true gland like formations, with or without papillary structures. Microscopically they exhibited both semimalignant and complete malignant characteristics. In a few the proliferation of epithelial cells was scant but sufficiently irregular and hyperchromatic to justify their classification under malignancy (Fig. 1). Many presented a dense stroma with invasion by surface cells (Fig. 2). Numerous mitoses, round cell infiltration, hyperchromatism, obliteration of cystic cavities by diffuse sheaths of cells (Fig. 3) together with pseudo-alveolar spaces formed by liquefaction necrosis (Fig. 4) furnished a variety of histological pictures. Bell concludes an accurate description of the malignant papillary neoplasms by saying "often the stroma is clear and the epithelium pleomorphic. Cystic cavities may contain either mucoid (Fig. 5) or serous secretions. This mucoid type of cell does not necessarily indicate a müllerian duct rest or an endodermal component of an embryoma. Germinal epithelium may be responsible."

2. Since hardly two *carcinoma* cases resembled one another a subdivision into four types seems necessary.

a. Under the *medullary* type are grouped those cases presenting anastomosing columns of epithelial cells which may vary as to size, shape, and staining characteristics. The stroma may be dense and cellular or loose with mucoid degeneration (Fig. 6). One may see cells like ova which Ewing attributes to mucoid degeneration and sheaths of squamous cells produced by metaplasia. Cystic areas when found are due usually to liquefaction and necrosis. The presence of goblet cells in the ovary does not necessarily indicate a met-

astatic tumor or fetal müllerian-duct rests. Walthard has demonstrated their presence in small islands in many otherwise normal ovaries and attributes them to metaplasia of germinal epithelium.

b. *Alveolar* formation of cells varies in all histological aspects from small round cells with deeply staining granular protoplasm arranged about an indefinite lumen (Fig. 7) and resembling lymphosarcoma, to larger clearer and more irregular cells arranged about a more definite lumen. The stroma is as variable as in the medullary type and may closely resemble a mesoblastic tumor of almost any variety.

c. *Granulosa cell* carcinomas are not common and are relatively benign because they are very often permanently cured by removal (Tausig). They consist of cells closely related to the granulosa cells and are classified by Carl Sternberg as epithelial tumors. Their origin from embryonic rests of ovarian parenchyma in the medulla of the ovary has been voiced by Telinde. King has stated they possibly arise from cells in the ovary which are the progenitors of these follicular cells. According to Flachel both the granulosa and the stroma are formed by the ovarian mesenchyme. Novak states "in either event the kinship of the two tissues is so close that tumors arising in the early stages of differentiation may assume the type of either carcinoma or sarcoma." Histologically they usually present a very constant picture. Masses of regular clear cells which resemble the granulosa cells of the graafian follicle, are arranged in a fairly loose formation about spaces which are often filled with bloody material (Fig. 8). A typical cylindrical formation of these cells is often present (cylindroid epithelioma, Fig. 9). A very unripe type of cellular formation may be present, which may closely resemble a sarcoma (Fig. 10). Careful examination, however will reveal the epithelial character and attempt at typical grouping on the part of the malignant cells. Also scattered throughout the tumor may be seen spaces resembling the Call and Exner bodies and theca folliculi. Novak described cells resembling secretory cells and decidua in two granulosa cell tumors, one reported by Arnold et al and the other by Dworzak.



Fig 1 Papillary cystadenocarcinoma showing early malignant changes Case 0095, age, 27 years, married, primipara, alive and well 8½ years after bilateral ovariectomy and irradiation

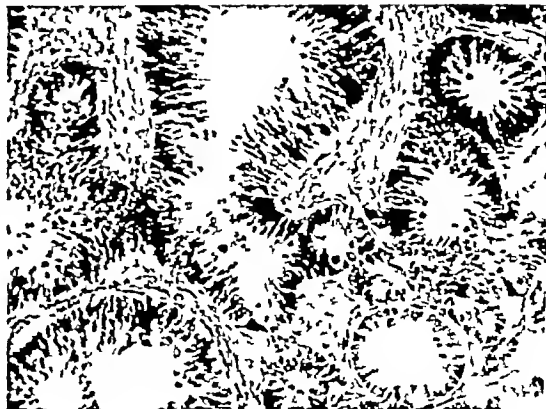


Fig 2 Adenocarcinoma Case 15588, age, 30 years, single, nullipara, died 10 months after bilateral cystic ovarian tumors were removed and irradiation therapy begun

d The *embryonal cell carcinoma* (seminoma ovary) resembles in many ways the related type found in the testis. In some respects it may be hard to differentiate histologically from the diffuse unripe granulosa cell carcinoma. Two of our 3 cases were of this sort. Careful examination, however, failed to reveal the grouping of cells in the fashion which is so diagnostic of the granulosa cell carcinoma. Diffuse masses of epithelial cells of a definite embryonal character with little or no stroma and obliteration of ovarian structure predominated the picture (Fig 11).

Clinically this tumor does not induce any changes in the primary or secondary sex characteristics as compared to definite clinical syndromes often associated with granulosa cell carcinoma and arrhenoblastoma.

3 *Embryoma* represents a group of neoplasms composed of heterogeneous tissue elements. Shattock stated that an embryoma may be due to the fertilization of one of the primordial ova in the ovary of the developing embryo, the result being that the embryo gives rise to a second imperfect individual whose origin is not synchronous with itself but is of a later date.

Marchand theorized the possibility of the fertilization and development of polar bodies although there is practically no evidence in its favor, and MacCallum states that there may be multiple teratomatous tumors which could

not be explained on this basis, since at most there are two polar bodies. The latter author believes that the evidence in favor of the isolation of a blastomere as the origin of teratomatous tumors is much stronger than the preceding theories. It is the only type of tumor in which a true mixed carcinoma and sarcoma may exist (Heinrich). They are usually unilateral although 2 of our 7 cases were bilateral when operation was done. This may be due to metastasis of the malignant cells from one ovary to the other. Wilms considered solid embryoma as originally benign, only secondarily showing malignant changes, while Pfannenstiel, Ewing, Boyd considered these tumors malignant from the beginning.

The 7 cases in this series showed histological characteristics of several types: Spindle cell sarcomas (Fig 12 D), myosarcomas (Fig 12 A), myxosarcoma (Fig 13), adenocarcinoma (Fig 14 A), and medullary carcinomas were found. The possibility of metaplasia was carefully ruled out. Usually one type of cellular structure predominated, but the presence of bizarre combinations and the apparent mixed type of involvement satisfied us as to their ovulogenic origin.

#### INCIDENCE

An accurate figure cannot be given as to the incidence of primary ovarian malignancies. Reports from the literature are confusing due to the differences in classification, especially



Fig. 3 Adenocarcinoma. Highly malignant cells filling cystic area in loose and mucoid like stroma. Case 35, age, 43 years, married, nullipara, died 4 months after palliative operation and 3 months after radiation therapy was begun.

of the semimalignant or borderline cases. Stout at the Presbyterian Hospital found 5.3 per cent of all female cancer to be ovarian. Norris and Murphy (19) reported that their ovarian neoplasms constituted 7.7 per cent of all gynecological lesions of which 1.4 per cent were malignant. Percentages of incidence of malignancy in ovarian tumors by five different observers varied from 7.3 to 24.2 (7, 12, 13, 17, 20).

No attempt has been made to determine the incidence in this Institute. Many cases have been admitted and treated which are not here reported because pathological material is not available for study.

#### AGE

No age is excepted in the development of a malignant neoplasm of the ovary.

Three carcinoma patients less than 30 years of age have been treated at this Institute the youngest patient being 11 years old. The incidence of ovarian cancer is highest in the fifth and sixth decades of life. Between 40 and 59 years of age our incidence is 55.4 per cent.

Of our cases 39.7 per cent had had a natural menopause when admitted and 9.68 per cent had had a cessation of menses due to operation.

Our cases are grouped as in Table I. It is notable that 88.3 per cent of the adenocarcinoma group occurred after 30 years of age.

TABLE I—AGE INCIDENCE

Group	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89
Adenocarcinoma							18	
Carcinoma								
Embryoma						31	30	
Total								
Total per cent		17			47		24.6	
Group per cent								
Adenocarcinoma		20			66		63	
Carcinoma		37			33			
Embryoma								

	Adenocarcinoma	Carcinoma	Embryoma	Total
Group 10-29 years, per cent		13	28	
Group 30-39 years, per cent	41		66.6	
Group 40-49 years, per cent	41			
Group 50-59 years, per cent	25	33	31	27
Youngest 10 years			15	
Oldest 70 years	69	33	33	66

that number being equally divided in the 30 to 49 and 50 to 69 age periods. Of the carcinoma group 55.5 per cent occurred in the 30 to 49 year period while 33.3 per cent happened under 30 years. The greatest percentage (66.6) of the embryomas occurred between the ages of 30 and 49. All of the 6 cases were under 39 years.

Age statistics in the carcinoma group are

Age	Average years	Oldest years	Youngest years
Mucillary	36	46	30
Alveolar	4	5	13
Germinal	33	33	
Embryonal	3	4	3

Of the total number of cases under 30 years (7.3 per cent) the adenocarcinomas lead with 50.0 per cent. Embryomas make up only 12.5 per cent of this group and carcinomas 37.5 per cent.

The average age of the adenocarcinoma group is 45.8 years. This is 0.8 years higher than a corresponding figure for the carcinoma group and 14.9 years increase over the embryoma group.

A history of malignancy in the immediate blood relations was present in 7 adenocarcinoma cases (10 per cent) and 1 embryoma case (16.6 per cent).

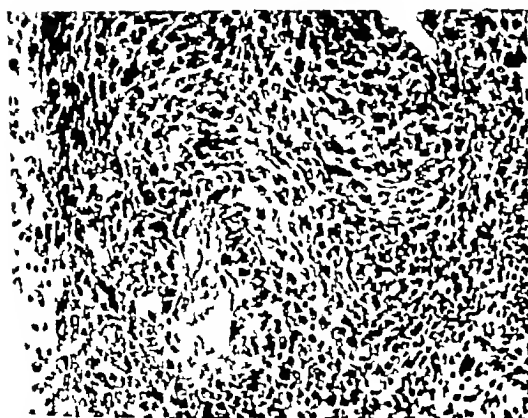


Fig 4 Both pictures show diffuse mass of round and spindle shaped cells in the wall of tumor and also pseudo-alveolar areas. Other sections showed typical adenocarcinomatous structures. Case 1366, age 58 years, single, nullipara, died 3 months after palliative operation for bilateral ovarian adenocarcinoma and 3 months after irradiation.

#### MARRIAGE AND PREGNANCY

Our statistics (Table II) show that of the total number 73.9 per cent are married. The figures for the individual groups vary from 61.1 per cent (carcinoma) to 83.3 per cent (embryoma) with the adenocarcinoma group having a percentage of 76.5.

In 34.7 per cent of our cases patients were never pregnant. In this respect the carcinoma group leads with a percentage of 38.8. Sixteen adenocarcinoma cases (23.5 per cent) and one embryoma case (16.6 per cent) were sterile in marriage. The largest number of pregnancies were

Group	Greatest number	Average
Adenocarcinoma	5	2
Carcinoma	10	4
Embryoma	6	4

A comparison of the four types of carcinoma follows

Type	Cases	Single	Married	Nullipara	Primipara	Multipara
Medullary	4	2	2	2	1	1
Alveolar	4	1	3	1	0	3
Granulosa cell	7	4	3	4	0	3
Embryonal cell	3	0	3	0	1	2

Abortions and miscarriages which in the great majority were apparently not induced, occurred in 23.5 per cent of the adenocarcinoma and 16.6 per cent of the embryoma and carcinoma groups. Of the last group (3 cases) 1 occurred in an alveolar type and the other 2

in the granulosa cell type (66.6 per cent of the married cases).

Only two stillbirths were recorded. One was an alveolar carcinoma and the other an embryonal cell type of carcinoma.

These figures testify as to the functional activity of the ovaries both in a normal and abnormal fashion.

#### SYMPTOMS AND SIGNS

Clinically these tumors presented a marked variety of symptoms and signs. None is in itself absolute for diagnosis. Only pathological study determines definitely their malignant qualities, although at operation one may identify cancer in many cases.

The prediagnostic length of symptoms averages about the same in all groups.

Name	Average months	Longest years	Shortest month
Adenocarcinoma	15	20	1
Carcinoma	11.6	3	1
Embryoma	13.5	2.5	1

Kaplan reported that the average duration of symptoms of ovarian malignancy in his series is 10 months with 1 case of 12 years.

Pain in the abdomen is the most outstanding symptom. Frequently it is hypogastric in type and many times is associated with nausea and emesis. Swelling of the abdomen is quite prevalent as are backaches, bearing-down sensations in pelvis and frequent and painful micturition. Loss of weight is often



Fig 5 Adenocarcinoma, mucoid type (radioresistant). Case 70 age 45 years, married, multipara, died year 20 months after palliative operation for ovarian to some mass and commencement of irradiation.

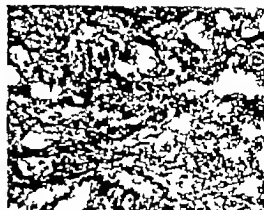


Fig 6 Medullary carcinoma with mucoid degeneration. Case 1606 age 30 years, single nullipara, died 14 years after right ovarian tumor was removed and 1 year after irradiation was begun.

marked. Menstrual irregularities with increased or decreased flow are not so frequent as a large percentage of patients are past the menopause. In these cases one often sees bloody vaginal discharge. When this postmenopausal bleeding is of the endometrium and more especially if it is periodic in character granulosa cell tumor of the ovary must be entertained. In this series 30.4 per cent had passed an apparently normal menopause when symptoms began. Mullerheim has reported 2 cases of ovarian cancer in women aged 60

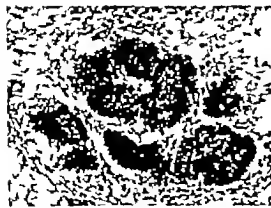


Fig 7 Alveolar carcinoma. Small round anaplastic epithelial cells resembling in some sections lymphosarcoma. Attempt to an management about an indefinite times. Case 1502 age 55 years, married multipara, died year after irradiation was begun and 1 month after diagnostic operation.

and 72 years who had swelling of both breasts. We have not noticed this in our cases. Precocious puberty with aggravation of secondary sexual characteristics may be seen in granulosa cell carcinoma in young girls. Two of our patients 11 and 14 years of age began menstruating when 11 and 12 years old respectively with early pubertal characteristics.

A comparison of clinical data in the three main divisions is interesting (Table III).

Pain in the abdomen was an outstanding complaint in 83.3 per cent of the embryoma cases and 77.7 per cent of the carcinoma cases, while enlargement of the abdomen showed a percentage incidence of 16.6 per cent and 37.7 per cent respectively. The adenocarcinoma group differed quite markedly in that the percentage of incidence of abdominal pain was 55.8 per cent and of enlargement of the abdomen 44.1 per cent. This latter complaint showed as either a diffuse growth or expansion of the abdomen with fullness, or else as a more unilateral suprapelvic enlargement.

Nausea, emesis, and headache were much more frequent in the carcinoma and embryoma groups. No histories of urinary disturbances were obtained in the embryoma cases but 25 per cent of the carcinoma and 14.7 per cent of the adenocarcinoma cases complained of frequent and painful micturition. Whitehouse cites the occurrence of painful as well as frequent urination as a differen-

TABLE II —MARRIAGE, PREGNANCY,  
MENOPAUSE

	Adenocarcinoma		Carcinoma		Embryoma		Total	
	No	Per cent	No	Per cent	No	Per cent	No	Per cent
Single	16	23.5	7	39.8	1	16.6	24	6.0
Married	52	76.5	11	61.1	5	83.3	68	71.9
Primipara	1	17.6	1	11.1	1	16.6	3	16.3
Multipara	24	35.2	0	50.0	3	50.0	27	30.1
No pregnancies—single and sterile cases	32	33.0	7	38.8	2	33.3	41	44.7
Sterile in marriage	16	23.5	1	16.6	1	16.6	18	18.4
Natural menopause	33	48.5	3	16.6	1	16.6	37	41.7
Surgical menopause	5	7.3	2	11.1	1	16.6	8	8.7
Symptoms after menopause	27	39.7	1	5.5	1	16.6	29	31.4

ADDITIONAL DATA ON MENOPAUSE

	Adenocarcinoma years	Carcinoma years	Embryoma years
Natural menopause			
Average age	47.6	44.6	45
Oldest age	58	53	45
Youngest	33	36	45
Surgical menopause			
Average age	42.4	44.5	
Oldest	49	44	
Youngest	39	39	
Symptoms after			
Menopause average	8.7	1	
Longest interval	0	1	
Shortest mos	1	1	

tial point in favor of malignancy in an ovarian tumor

Menstrual disturbances, such as irregular periods, profuse flow, and pain were not present in the embryoma group although 2 of the 6 cases had a leucorrhoea previous to admission. Menstrual irregularities for variable lengths of time previous to admission were noted in 16.1 per cent of the adenocarcinoma cases and 5.5 per cent of the carcinoma cases. Two of the adenocarcinoma group had quite severe pain on menstruating since the onset of their disease. Vaginal bleeding between periods but usually following menopause was present in 17.6 per cent of the adenocarcinoma cases and 27.7 per cent of the carcinoma group. It has been noted by other observers (Schroeder, Tietze) that in cases of ovarian malignancy a hyperplasia of the endometrium often takes place. This is especially true of the granulosa

TABLE III —SYMPTOMS

Symptoms	Adenocarcinoma		Carcinoma		Embryoma		Total	
	No	Per cent	No	Per cent	No	Per cent	No	Per cent
Pain in abdomen	38	55.8	14	77.7	5	83.3	57	61.9
Enlarged abdomen	30	44.1	5	27.7	1	16.6	36	39.1
Nausea and emesis	1	1.5	4	22.2	2	33.3	7	7.6
Backache	13	19.1	6	33.3	3	50.0	22	23.8
Headache			2	11.1	1	16.6	3	3.2
Loss of weight	12	17.6	2	11.1			14	15.2
Pain in rectum			1	5.5			1	1.1
Blood from rectum	2	2.9	1	5.5			3	3.2
Urinary disturbance frequency pain	10	14.7	4	22.2			14	15.2
Constipation	2	2.9					2	2.2
Gain in weight	2	2.9					2	2.2
Irregular menstrual periods	11	16.1	1	5.5			12	13.0
Pain on menstruating	2	2.9					2	2.2
Amenorrhea (recent)	2	2.9					2	2.2
Never menstruated					1	16.6	1	1.1
Vaginal bleeding	22	32.7	5	27.7			27	29.1
Leucorrhoea	19	27.6	5	27.7	2	33.3	26	28.1
Miscarriage or abortion	16	23.5	3	16.6	1	16.6	20	21.7
Stillbirths			2	11.1			2	2.2

cell carcinomas. E. S. J. King explains this hyperplasia and also endometriosis by a hormonal action. He says "It is possible that tumors consisting of cells which are closely allied to the granulosa cells—and therefore are presumably capable of producing the follicular hormone—which may be abnormal, either in amount or quality—may have a considerable effect on the endothelium e.g., overgrowth. It has been shown that em-

TABLE IV —AGE MENSTRUATION BEGAN

	Adenocarcinoma 68 cases	Carcinoma 18 cases	Embryoma 6 cases	Total	Per cent
Age in years					
11	4	2	0	6	6.52
12	13	3	1	17	19.5
13	21	3	2	26	28.2
14	12	5	1	18	20.6
15	8	2	1	11	12.0
16	9	1	0	10	11.3
17	2	1	0	3	3.26
18	0	2	0	2	2.17
Average age	13.9	14.7	13.5	14	
Youngest	11	11	13	11	
Oldest	17	18	15	18	





Fig. 8. Granulosa cell carcinoma. A, left, Menstrual tissue of regular, round, somewhat clear cells tending to group in cylinders and about pseudo alveoli. B, cells arranged about blood spaces. Case 7076 age 3 years, single, nullipara alive 43½ years after right ovarian tumor was removed (granulosa cell tumor). 34 years after left ovarian tumor was removed (granulosa cell carcinoma). 34 years after irradiation was begun.

zyonic tissue contains the hormone so therefore anaplastic type cells must contain an additional amount.

Novak reported a case in which after removal of a granulosa cell tumor the patient complained of a second menopause due to cessation of folliculin secretion. He says that this clinical syndrome has been described in only one other case (Schulze's case).

One of our granulosa cell carcinoma cases gave a history of periodic uterine bleeding beginning 1 year after a normal menopause. She was admitted to the Institute in a moribund condition and died in 6 days after receiving one X-ray treatment. Autopsy revealed an extensive tumor involving both ovarian regions and extending to the umbilicus.

Two adenocarcinoma patients had never had a menstrual flow due to age at onset of tumor growth.

Physical examination may not reveal the true character of the lesion. A palpably free mass, or a so called frozen pelvis with ascites and diffuse abdominal enlargement may be present. Even after metastasis has taken place, a malignant tumor may remain movable if pedunculated (Ewing). Many times pelvic examination affords little information as to which ovary is involved as either may be displaced.

On operation it was found that 72.47 per cent of the cases had growths in both ovaries.

Shaw reported 76.7 per cent bilateral involvement and said: "If bilateral ovarian tumors are found at operation the chances are nearly 5 to 1 in favor of the tumors being malignant."

One rarely sees distant metastasis in ovarian cancer because the majority of these tumors spread by implantation. Four adenocarcinomas and embryoma showed distant metastases. Shaw's observation that one may not find evidence of metastasis in cases of bilateral malignant tumors and that they may arise independently of one another seems logically true. Ewing states: "The majority of carcinomas are originally bilateral or soon become so."

The percentages of bilateral involvement of the cases in this series at operation are:

	Percent
Adenocarcinoma	80.9
Carcinoma	55.5
Embryoma	33.3

#### TREATMENT

The judicious use of a combination of surgery and irradiation remains the best method in the treatment of malignant neoplasms of the ovary. With the knowledge that an ovarian tumor is malignant at the time of operation, it is justifiable to remove the other ovary, uterus, tubes, and broad ligaments, even though these structures are apparently normal in appearance and the patient is in the reproductive period of life. When widespread

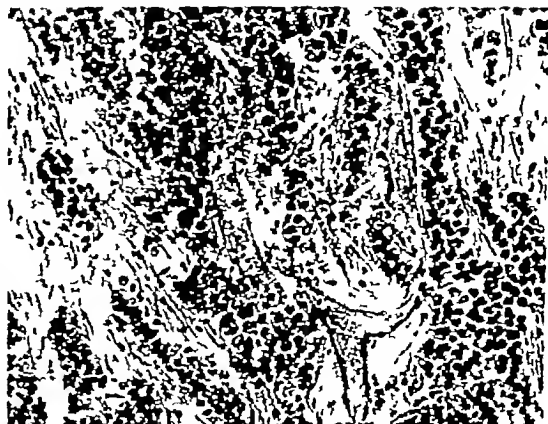


Fig 9 Granulosa cell carcinoma A, left, Groups of cells in loose formation, B, masses of cells in cylindrical formation and about blood spaces Case 8147, age, 41 years, single, nullipara, died 9 years after palliation operation for ovarian tumors and irradiation (cause of death—cerebral hemorrhage), very radiosensitive

metastasis is present Keene Pancoast, and Pendergrass have found in unusual cases "rather marked improvement in general health and retardation of the malignant process" by excision alone of the primary growth. Since any such case in our series has been irradiated following operation, improvement, when noted was credited to the radiation therapy. It is apparent that many of these metastatic cases, even when only a diagnostic laparotomy has been performed show a marked palliation of symptoms and prolongation of life following treatment by irradiation therapy.

In discussing the value of irradiation in the treatment of ovarian tumors it is essential to know the type and extension of the neoplasm. Morphologically similar tumors may show a difference in their response to radiation therapy. It is apparent that there exists an individual variation in the reaction of the tissue bed to irradiation.

Irradiation treatment in this Institute was carried out by means of X-ray and radium, separately, or in combination.

**X-ray** Prior to 1921 medium voltage X-ray with aluminum filter was used. Three of the adenocarcinoma cases and one of the embryoma cases were treated in this manner. It is apparent now that the doses which were used at that time were inadequate. Since 1921 high voltage X-ray therapy has been used. The factors are

Volts	200,000
Milliamperes	30
Distance	80 centimeters
Angle	90 degree
Field size	20 by 25 centimeters
Filter—copper	5 millimeter
aluminum	10 millimeter

The tumor dose was computed from the patient's pelvic measurement by means of isodose charts. Cross fire was accomplished through two portals—anterior and posterior—in divided amounts sufficient to produce a skin erythema dose, which in this Institute represents 800 roentgens (air scattering) and 1130 roentgens (tissue scattering). The course was usually repeated in 2 months if the patient's condition warranted. As many as 6 courses have been given within a period of 3 years. Occasionally more than two fields were used.

**Radium packs** Radium packs prior to 1931 were used at 6 centimeters distance with a filter of 2 millimeters of brass, 0.5 millimeter of silver, 1 millimeter of aluminum and 1 centimeter of rubber.

The size of field was 6.5 by 7.5 centimeters through 2 or 3 portals, anterior and posterior, and sometimes perineal. Doses were as high as 26,420 milligram hours in one course.

Since 1931 the 4 gram radium element pack has been used. When two fields—anterior and posterior—were used at 10 centimeters' distance, dimensions of field size were 20.5 by 20.5 centimeters. Occasionally two anterior



Fig Granulosa cell carcinoma. More sarcoma type with some lymphoid stroma. Case 9124, age 1 years, single nullipara, died 6 months after left ovarian tumor was removed and 3 months after irradiation was begun.



Fig Embryonal cell carcinoma. Case 38, age 4 years, married nullipara, died 3 years after an operation for the removal of an unilateral ovarian tumor was performed and treatment by irradiation therapy was instituted.

two posterior and one perineal field were used at 10 centimeters distance. Here the field size was 10 by 10 centimeters. Filter was 1 millimeter of platinum 1.5 millimeter of steel with a secondary filter next to the skin of 0.5 millimeter of copper and 1.0 millimeter of aluminum. The dose has been as high as 705,000 milligram hours given in 5 courses of 10 treatments each alternating anterior and posterior over a period of 9 months.

**Intracavitary.** Before 1931 radium emanation was used in two 50 millicurie tubes placed in tandem into cervix uteri. Dose varied from 1200 to 2400 millicurie hours. Filter was 0.5 millimeter gold 0.5 millimeter brass, and 1.0 millimeter rubber. Since 1931 radium element has been used in a 100 milligram tube. Filter 1.0 millimeter platinum and 1.0 millimeter aluminum. Dose from 1200 to 2400 milligram hours.

Nine cases received this type of therapy in conjunction with radium pack or X-ray therapy.

**Interstitial.** In a few cases radon seeds were placed in the cervix uteri for local conditions of the cervix at the time diagnostic curettage or biopsy of cervix was done. This was always in conjunction with external irradiation.

Two of the cases received pre-operative irradiation only due to the advanced condition of involvement. One was an adenocarcinoma and the other an alveolar carcinoma.

One embryoma case received both pre-operative and postoperative irradiation.

#### RESULTS

It is very difficult to reach any positive or detailed conclusion as to end results in cases of intra abdominal malignancies. This is especially true for those tumors affecting the ovary since each case is an integral cancer study in itself. Not only do the tumors of the same group differ in many pathological respects but there is a great variation in the duration of the growth before the first symptoms are noticed. Any predisposing factor such as a benign neoplasm or a fetal inclusion may obscure the clinical history before a diagnosis is made. Even surgical intervention is not always adequate in those cases in which complete extirpation of the tumor is recorded. The radiosensitivity of the malignant cells is no more important than the reactionary power of the host to the irradiation. It is apparent that all these factors enter into any discussion of results which are measured according to length of life not only following complete or incomplete operation but also following treatment by irradiation.

According to these two headings the three main case groups have been divided into those who are alive or dead following complete or

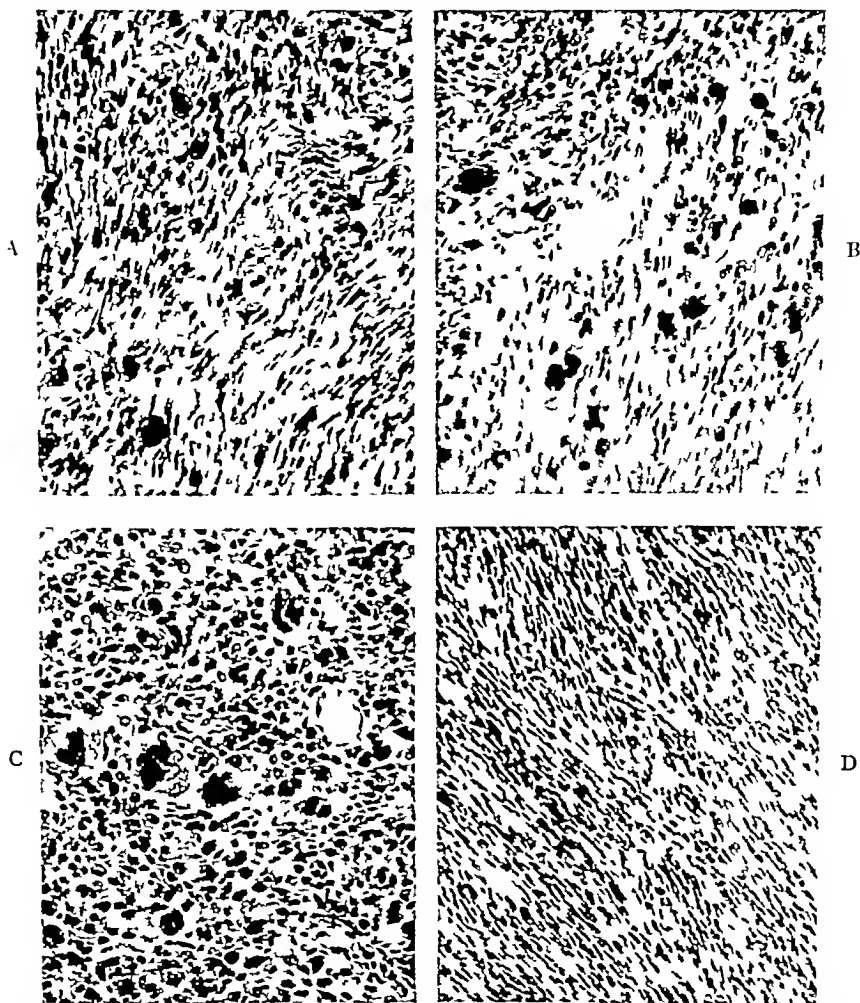


Fig 12 Malignant embryoma. Shows giant cells epithelium like cells, and spindle cells in variety of stroma. Case 6402, age, 38 years, married, multipara 3, died 1 year, 8 months after removal of unilateral ovarian tumor and 1 year, 7 months after irradiation was begun.

palliative (or diagnostic) operations. Notice was made as to whether the growth at operation was bilateral or unilateral (Table V). In most cases treatment was begun soon after operation. There are 3 cases, however, in which irradiation was given before the abdomen was opened for pathological examination. This was due to the fact that the clinical evidence was strongly in favor of extensive malignancy. This accounts for the longer length of life period in those cases following treatment than the same cases following operation. The

end-results for those cases in which complete operation was performed are much better than those in which only palliation was accomplished. Of course this latter group came to the surgeon much too late but some effort may be made at appraising the irradiation effect.

In comparing the three main groups, it is found that the adenocarcinoma cases have not only a longer average life period following operation and treatment but also present the longest case survival—10 years. But the per-



Fig. 3. Malignant embryoma. A, left, Shows syncytiotrophoblastic giant cells. B, shows spindle cells and areas with macerated stroma. Case 780 age 34 years, married multipara 4.

centage of the patients who are alive is only 18.8. This may be explained by the clinical fact that late recurrences are the rule and not the exception (Thibaudreau) thus cutting down the percentage of live cases while the duration of life is increased. This does not compare favorably with the corresponding percentage in the carcinoma group (50 per cent).

The following chart shows not only this, but also the percentage alive and without evidence of recurrence.

Group	Cases	Alive		Alive and without recurrence	
		No.	Per cent	No.	Per cent alive
Adenocarcinoma	66	12	18		28
Carcinoma	18		90		55
Embryoma					

In analyzing the several groups, we attempted to correlate the histological findings with the end results of operation and irradiation.

**Adenocarcinoma.** The longest case survivals were those in which complete removal of the tumor was accomplished and in which the histological section showed a low grade of papillary adenocarcinoma with psammoma bodies (Fig. 15). Of the 3 patients who lived 3 years or longer following operation and treatment 6 were of this type.

There are however cases in which a pronounced malignant picture is present and still

the patient survives over the 3 year period. This is especially true for those types in which widespread involvement has not yet taken place. The large doses of radiation which these cases had certainly were factors in prolonging life.

Many patients come to operation too late (Fig. 16). In these patients only palliation or diagnostic procedures were attempted. Ample clinical evidence is obtained in this group in respect to the radioresistance of most ovarian adenocarcinoma cases.

Even in the case of a well formed adenocarcinomatous structure in which the tumor is apparently adequately removed one may see irradiation to be of little effect in preventing recurrences.

It is apparent that there is no positive criterion in prophesying the prognosis. The more malignant types tend to be further advanced at time of operation and in many cases in which a complete removal of a unilateral ovarian tumor is recorded extension to the other ovary may already have taken place without its gross alteration. Or else, tumor cells remain in the mesovarian or broad ligament. It may be that those patients who survived the longer periods were more sensitive as hosts to the irradiation treatment. The gross and histological characteristics do not offer any basis for determining the relative radiosensitivity of these tumors. It is safe to say that early operation in which complete

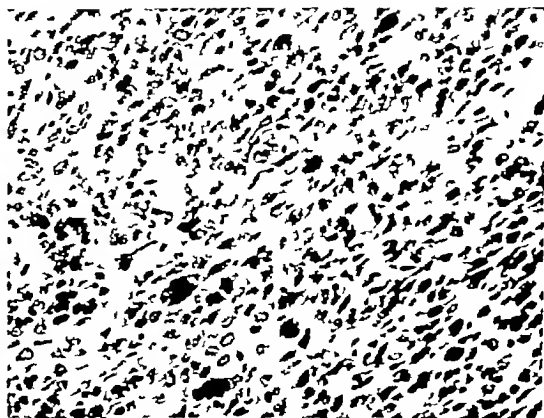


Fig 14 Malignant embryoma A, left, Shows adenocarcinoma of ovary found at operation, B, shows embryoma of ovary found at autopsy Case 13398, age, 33 years, married, multipara 6, died 3 years after irradiation was begun and 2 years, 10 months after bilateral ovarian tumors were removed

excision of both ovaries is possible and full tumor doses of irradiation remain the best methods of treatment

**Carcinoma** Since the tumors differ widely in their pathological characteristics, each subgroup will be considered separately

1 *Medullary type* Of the 4 cases recorded only one is alive and apparently without signs of recurrence The average length of life for those who are dead is 12 years the longest and shortest being 2 years and 5 months, respectively The former case died of chronic nephritis while the latter appeared too far advanced to discredit radiation treatment A

third case which survived for 1 year after treatment had a carcinomatous tumor showing mucoid degeneration (Fig 6) Of course this was radioresistant The surviving case had bilateral tumors removed and has received 1423 r (tissue scattering) An adequate surgical removal plus this irradiation has so far kept the patient free from recurrence for 3½ years

2 *Alveolar type* One case is alive and apparently without recurrence for 10 months The 3 other patients are dead The length of life averaged about 7 months, the longest being 1 year (Fig 7) and the shortest 4 months

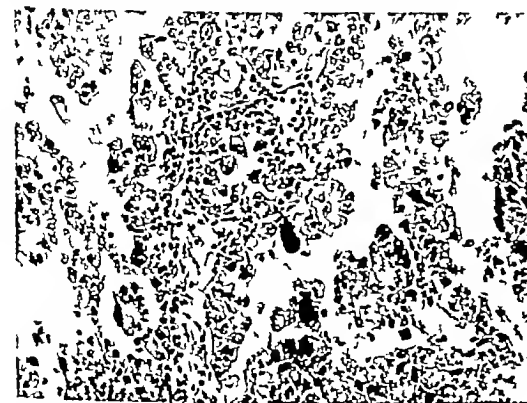


Fig 15 Papillary cyst adenocarcinoma of low grade malignancy Shows psammoma bodies Case 12404 age 48 years, married, multipara 2 alive and without evident recurrence 4 years 8 months after irradiation and 5 years 2 months after removal of a unilateral ovarian tumor

Fig 16 Adenocarcinoma Very malignant with wide spread metastasis Case 12946, age 50 years, married, nullipara died 2 months after a diagnostic laparotomy had been performed and irradiation therapy had been instituted

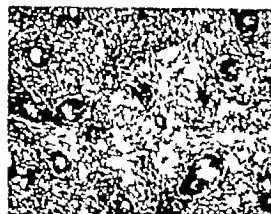


Fig. 7 Granulosa cell carcinoma. Resembles in some respects antral folliculars. Case 90, 8 yrs., 45 years, married, multipara, died 6 months after an operation for the removal of an unilateral ovarian tumor and 4 months after irradiation had been instituted.

In all these cases the cells were of a marked malignant quality. Their response to irradiation was poor. The 1 case alive in which bilateral ovarian tumors were removed has felt well. She has received 110,000 milligram hours of radium pack. It may be that surgery was adequate. The microscopical structure of the tumor showed radiosensitive qualities. It is too early to appraise any results in this case.

3 *Granulosa cell type*: Three cases are alive and without evidence of recurrence for the

following lengths of time after treatment was begun: one for 3 years and two for 1½ years. Both of the latter 2 cases are interesting in showing late recurrence. Four cases are dead—lengths of life being 9 years (died from cerebral hemorrhage), 4 months, 13 months, 6 days after treatment was begun following operation. The first case (Fig. 9) had a palliative operation which was followed by three courses of radium pack which were given over a period of 3 years and two courses of deep X-ray therapy.

TABLE V A—POSTOPERATIVE LENGTH OF LIFE

Group	Type or dead	On interval or (date)	Removal of tumor						Palliative or diagnostic					
			No.	Average		Longest		Shortest	No.	Average		Longest		Shortest
				yr	mo	yr	mo			mo	yr	mo	yr	mo
Adenocarcinoma	Alive	U						6						
		B				10								
	Dead	U	6		6									
		B	14									4		days
Carcinoma	Alive	U						8						
	Dead	B												
Embryoma	Alive	U												
		B												
	Dead	U						8						
		B			10			10						



Fig 18 Papillary cystadenocarcinoma Shows malignant structure in wall of cystic tumor Case 7473, age, 29 years, married, primipara, died 5 years, 10 months after removal of a unilateral ovarian tumor and 5 years, 11 months after irradiation treatment was started

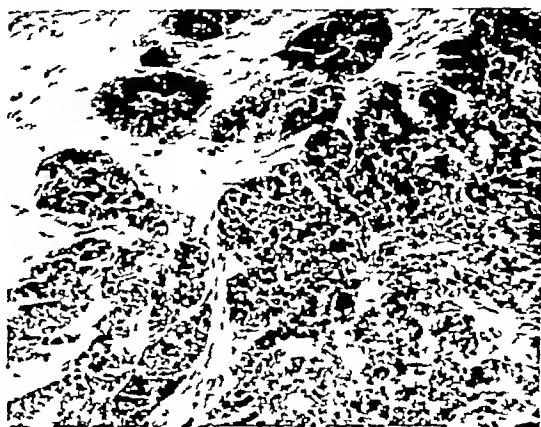


Fig 19 Adenocarcinoma Shows moderately well formed adenocarcinomatous formations Case 12377, age, 39 years, married, nullipara, died 3 years, 4 months after bilateral ovariectomy and 3 years after irradiation was begun.

The second case did not respond to irradiation. It does not present the typical granulosa cell carcinoma picture and has a great amount of dense stroma (Fig 17). In some respects, it resembles the oophoroma folliculare type of tumor. This patient died 4 months after a total of 1152 r (tissue scattering) in 4 treatments in 8 days was given over pelvis for a large tumor mass in the posterior cul-de-sac.

The third case, an 11 year old girl with an unripe granulosa cell carcinoma (Fig 10) after a diagnostic operation received a total of

2576 r (tissue scattering) in two courses 7 months apart. She died 13 months after admittance X-ray, although not curing this girl, proved very palliative and no doubt was responsible for prolonging her life.

The fourth patient was admitted in an almost moribund condition and after receiving one X-ray treatment (565 r tissue scattering) died in 6 days. Autopsy revealed a large tumor mass in the pelvis extending to the umbilicus. Section proved the growth to be a granulosa cell carcinoma.

TABLE V, B—POSTADMISSION (TREATMENT) LENGTH OF LIFE

Group	Alive or dead	Uni lateral or bilateral	Removal of tumor								Palliative or diagnostic							
			No	Average		Longest		Shortest		No	Average		Longest		Shortest			
				yr	mo	yr	mo	yr	mo		yr	mo	yr	mo	yr	mo		
Adenocarcinoma	Alive	U	4	3	6	3	6	2	6									
		B	9	3			6		2									
	Dead	U	8	1	1	2	6		2	1	2	8	2	8	2	8		
		B	22		10	3		2	24		9	6				2 days		
Carcinoma	Alive	U	5	2	6	2	10	1										
		B	4		8		10		6									
	Dead	U	3		9	1	1		4									
		B	1	3		3		3		5	2	7	9			4		
Embryoma	Alive	U																
		B																
	Dead	U	3	1		1	6		6	1		2		2		2		
		B	1	3		3		3		1		4		4		4		



4. *Embryonal cell type* This is a comparatively radiosensitive tumor. Stewart has stated that massive regression may be expected but massive recurrence with gradually increasing resistance has occurred. At the Memorial Hospital this class of case had not been successfully controlled. We have only 3 cases. Two are alive and without evidence of recurrence 1 for 2½ years and the other for 1½ years. The 1 who is dead lived for 3 years after X ray therapy was begun (Fig 11). She died from bowel obstruction.

From these few carcinoma cases, it is not possible to draw any definite conclusions as to radiosensitivity. It may be stated however that the embryonal carcinoma and the granulosa cell carcinoma are more radiosensitive than the medullary and alveolar types. Also since recurrence is common, even after a so called complete extirpation of a tumor irradiation is indicated. The tumors vary as to their response to this irradiation. The granulosa cell carcinomas, when of a more ripe character offer more possibilities for cure from surgery and irradiation than the unripe types.

*Embryoma* Every one of the embryoma cases presented a different histological picture. All the patients are dead. One patient lived 3 years after admission and 2 years, 10 months, after operation. The average length of life for all the others was less than 1 year the longest being 18 months and the shortest 2 months. In none could one determine what the outcome might be from the gross or histological involvement. As is true for all malignant embryomas, one type of cell may predominate although in all of our cases a combination of cellular forms was present. This makes the estimation of radiosensitivity rather hard.

#### CONCLUSIONS

1. Primary malignant neoplasms of the ovary present a complex study due to the differences in research data regarding its embryology and histological transformations.

2. Most ovarian malignancies arise from germinal epithelium or from benign germinal epithelial tumors through malignant degeneration. Others arise from embryonic rests and ovulogenic neoplasms.

3. A division into three main groups and a pathological description of each type have been made.

4. From a survey of the literature and our own cases it is found that ovarian cancer is not uncommon and that no age is excepted. The greatest number occur between 30 and 60 years of age. Our extremes were 11 and 69 years of age.

5. In our cases 73.9 per cent were married, 55.4 per cent had been pregnant from one to ten times, the average being from two to four; 21.7 per cent had miscarriages or abortions; 23.5 per cent of the adenocarcinoma cases and 16.6 per cent of the embryoma cases were sterile in marriage; 39.7 per cent of the adenocarcinoma cases and one granulosa cell carcinoma had passed an apparently normal menopause when first symptoms occurred. These figures testify for the hormonal functional association in the etiology of ovarian cancer both in the normal and abnormal capacity.

6. Pre-diagnostic length of symptoms average from 11 to 15 months. They are most severe in the carcinoma group. Pain in the abdomen and enlargement of the abdomen are the outstanding complaints in all groups. The clinical picture is discussed with special reference to endocrinological syndromes of the granulosa cell carcinoma.

7. Results are judged according to length of life following complete or palliative operation for unilateral or bilateral tumors, and also following irradiation.

8. Best average results were in the adenocarcinoma group probably due to a number of early low grade malignant cases which furnished better surgical material.

The embryoma group yielded the worst end results.

Of the carcinoma group the alveolar type showed the poorest results. The granulosa cell and embryonal cell types were most favorable.

In all groups complete removal of tumors gave longer survivals than palliative procedures.

9. Differences in radiosensitivity are found. The best reaction to irradiation is important.

The granulosa cell and embryonal cell types

of carcinoma are most sensitive Both tend to recur

The low grade malignant type of adenocarcinomas offer the best results from surgery and irradiation in this pathological group Other adenocarcinomas tend to be radio-resistant, as do the alveolar and medullary carcinomas found in this series

10 Treatment to be adequate must consist of early surgical removal of both ovaries, followed by deep irradiation in large tumor doses

We express our appreciation to Dr A A Thibaudeau for his counsel on the pathological classification and to Mr William F Payne for the photomicrographs used in this paper

# REFERENCES

- 1 ARNOLD, W, MATTHIAS, C, and KOERNER, J Zur Pathologie der Gewächse mit morphogenetischen Einflüssen, Spätreizidiv einer Eierstockkrebs und Vergungung der Uterusschleimhaut Arch f path Anat., 1930, 277 48-68
- 2 BELL, W B Pathology and clinical features J Obst & Gynec., Brit Emp, 1931, 38 249-255
- 3 BOYD, W Surgical Pathology pp 216, 524 Philadelphia W B Saunders Co, 1925
- 4 DWORZAK, H Ueber einem Fall von Granulosazell tumor Zentralbl f Gynaek., 1932, 56 1033-1039
- 5 Ewing, J Neoplastic Diseases 3d ed Philadelphia W B Saunders Co, 1928
- 6 FISCHER, A Zur Eröffnung des neuen Institutes fuer Embryologie. Wien Klin Wchnschr, 1922, 35 355
- 7 FLEMING, A Clinical survey of a consecutive series of ovarian neoplasms J Obst. & Gynec., Brit. Emp, 1931, 38 280-301
- 8 HEINRICH Martin's Handbook, 1899, 2 539 Quoted by Ewing, loc. cit
- 9 KAPLAN, I. Report of over a thousand unselected cancer cases, treated in 1931-1932 at the New York City Cancer Institute, Welfare Island Radiology, 1933, 21 442-443
- 10 KEENE, F E, PANCOAST, H K., and PENDERGRASS, E P Value of irradiation in treatment of inoperable cancer of the ovary J Am M Ass, 1927, 89 1053-1055
- 11 KING, E S J The association of endometrosis with neoplasms of the ovary Surg, Gynec & Obst., 1929, 49 433-439
- 12 KUSUDO SHOHJ Statistischen und pathologisch anatomischer Beitrag zur Kenntnis des Ovarialtumoren Arch f Gynaek., 1925, 129 402
- 13 LIPPERT, W Beitrag zur Klinik der Ovarialtumoren. Arch f Gynaek., 1905, 74 389
- 14 MACCALLUM, W G Textbook of Pathology Philadelphia W B Saunders Co, 1925
- 15 MARCHAND Missbildungen Eulenberg's Realencyklopaedie, 1897, 15 503 Quoted by MacCallum W G loc cit.
- 16 MAXIMOW, A Textbook of Histology Philadelphia W B Saunders Co, 1930
- 17 MAYER, A Quoted by Norris and Vogt, loc. cit
- 18 MULLERHEIM, R Ovarialtumoren bei Greisinnen mit Hypertrophia der Mammæ und des Uterus und mit Uterinen Blutungen Zentralbl f Gynaek., 1928 52 689
- 19 NORRIS, C C, and MURPHY, D Malignant ovarian neoplasms Am J Obst & Gynec., 1932, 23 833
- 20 NORRIS, C C, and VOGT, M E Malignant ovarian neoplasms with a report of the end results in a series of 56 cases Am J Obst. & Gynec., 1925, 10 684
- 21 NOVAK, E Granulosa-cell carcinoma of ovary as a cause of post menopausal bleeding Am. J Surg, 1934, 24 595-610
- 22 PFANNENSTIEL, J Veit's Handb d. Gynaek., Wiesbaden, 1908
- 23 SAMPSON, J A Endometrial carcinoma of the ovary, arising in endometrial tissue in that organ Arch. Surg, 1925, 10 pt. 1
- 24 SCHROEDER, R Granulosazell tumor des Ovars mit glandularzystischer Hyperplasie des Endometriums und beginnendes Karzinom auf diesem Boden. Nordwestdeutsche Gesellsch f Gynaek., 1921, No 21 Quoted by Tietze, loc cit
- 25 SCHULZE Quoted by Novak, loc. cit.
- 26 SHATTOCK, C E An acornus embryoma consisting of a hydrocephalic fetal head contained within an ovarian cyst in a child 2½ years of age, ovariectomy Brit. J Surg, 1922-1923, 10 334-336
- 27 SHAW, W Pathology of ovarian tumors. J Obst & Gynec., Brit. Emp, 1933, 40 257-272
- 28 STERNBERG CARL. Halban und Seitz, Biologie und Pathologie des Weibes vol. 5, pt. 2, p 751-760 and 789-791
- 29 STEVENS, T G Tumors from pathological aspect. J Obst. & Gynec., Brit. Emp, 1931, 38 256
- 30 STEWART, F W Radiosensitivity of tumors Arch Surg, 1933, 27 979-1064.
- 31 STOUT, A. P Human Cancer Philadelphia Lea & Febiger, 1932
- 32 TAUSSIG, F Granulosa-cell tumor of the ovary (folliculoma malignum) Am. J Cancer, 1931, 15 1547
- 33 TAYLOR, H. C, JR. Malignant and semi malignant tumors of the ovary Surg, Gynec. & Obst., 1929, 48 204-230
- 34 TELLENDE, R. W Granulosa-cell tumors of the ovary and their relation to postmenopausal bleeding Am J Obst. & Gynec., 1930, 20 552
- 35 THIBAudeau, A A. Some pathological aspects of carcinoma of the ovary Arch Clin. Cancer Research 1926, March
- 36 TIETZE, K. Granulosazell tumor und heterotopie Tiefsenwucherung der Uteruse Schleimhaut. Ztschr f Geburtsh u Gynaek., 1927, 91 111
- 37 WALTHER, M Zur Aetiologie der Ovarialadenome Ztschr f Geburtsh. u Gynaek., 49 233
- 38 WHITEHOUSE, B Clinical aspects of ovarian tumors. J Obst. & Gynec., Brit. Emp, 1931, 38 264-273
- 39 WILMS, M Ueber die Dermoidcysten und Teratome, mit besonderer Berücksichtigung der Dermode der Ovarien Deutsch. Arch. f klin Med, Festschr Leipz, 1895, 55 289-396

HYPOPLASIA OF THE KIDNEY<sup>1</sup>

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THE difficulties encountered in attempts to decipher the pathological alterations and embryological defects of kidneys of the type usually classified as rudimentary hypoplastic or aplastic kidneys, are probably directly related to the confusion that exists in the literature on hypoplasia of the kidney. Congenital atrophy, aplasia, agenesis, rudimentary and infantile kidney are names used and not infrequently without strict adherence to the pathological definitions of hypoplasia, aplasia and acquired disease.

At the present time it seems best to separate these kidneys into two main groups. One group would include all kidneys altered by acquired diseases such as inflammation, circulatory disturbances, trauma, and hydronephrotic obstruction. Regardless of the time such changes occur, whether in fetal or post fetal life, the name should include the concept of acquired atrophy. The other group would comprise all kidneys altered because of hypoplasia or aplasia of the metanephric mass, the derivatives of the primary excretory duct or those of the vascular elements. Hypoplasia would be used when there is a diminution in size due to decrease of the number of cellular

elements or decrease in the size of the cells or both. Aplasia would be properly used when there are no remnants of these original structures.

It is usually difficult to separate acquired atrophic kidneys from the hypoplastic or the aplastic kidneys because subsequent disturbances from inflammation from circulatory disturbances, or from hydronephrotic obstruction frequently alter the latter type. For this reason, histological standards for differentiating the two should be emphasized so that a more definite basis for diagnosis is made available.

The three renal malformations described herein seem to offer good criteria for some of these differentiations. In the first instance, aplasia of the elements derived from the metanephric mass best explains the characteristics of the kidney. In the second instance, bilateral complete hypoplasia of all of the elements derived from the primary excretory duct offers a satisfactory interpretation of the alterations. In the third instance the changes are limited to the superior calyx of the kidney and here also hypoplasia of part of the elements derived from the excretory duct is most consistent with the essential features of this pathological malformation.

The clinical diagnosis of the congenital hypoplastic kidney is often difficult and of considerable importance in renal surgery because it alone will not sustain life and not infrequently due to acquired disease is a source of danger to the other kidney.

Hypoplasia of the kidney was known to Blasius in 677. Ballowitz (1895) assembled 20 cases, Riad (1903) 36 cases. Since that time many cases have been added to the literature some of which are definitely hypoplastic, whereas others should be classified as acquired atrophy or one of the other forms of congenital anomaly.

According to Papin hypoplastic kidneys are more frequently found in men than women, and the right side is more often



Fig. Case. Retrograde pyelogram demonstrating an elongated, rudimentary right renal pelvis with an upper protruding superior calyx.

affected. It has been found in all ages, from the fetus to advanced life. In the living, it is always unilateral since if bilateral, it could not sustain life. It may lie in a normal position or may be ectopic. The renal pelvis is usually small and frequently cone shaped with small calyces, some of which may be rudimentary in type.

The ureter is often small, and may even be obliterated. In some cases it is normal, dilated, anomalous, or entirely absent. The vessels of the renal pedicle are small in many instances, but at times normal in appearance, in others obliterated or absent.

As a rule the opposite kidney is hypertrophied, but in some cases it may appear to be normal or smaller in size. Associated anomalies of the genito-urinary tract are not infrequent findings.

The embryological arrest that causes renal hypoplasia may involve the nephrogenic tissue, the wolffian duct, or both (Papin). The symptoms may be few and difficult to interpret, reduction or absence of function being the only sign. The symptoms may be referred

to the opposite side. The signs and symptoms of almost any renal disease may be found in these cases. The diagnosis is often difficult. The roentgenological examination may show one large and one small kidney. The pyelogram may visualize a rudimentary type of pelvis. The cystoscopic examination may show changes in the trigone and the ureteral orifices which may be helpful in making the diagnosis.

The functional test is of value in that the function of the affected side is reduced or wanting. The opposite kidney, which is usually the seat of compensatory hypertrophy, must bear the entire excretory burden and, from a surgical standpoint, must be considered a solitary kidney.

**CASE 1.** A woman, aged 28 years, on admission to the hospital, stated that she had suffered from cystitis since childhood. These attacks were intermittent and often ushered in with chills and fever, frequency, and urgency. She had been treated with various forms of medication which gave only temporary relief. She had always been underweight, and had been unable to overcome this after making many efforts. She had pain in both flanks which varied in intensity and was more often felt on the right side. Pus was found in the urine on many occasions and she thought her urine always contained some pus. She had never had any hematuria.

Physical examination disclosed a tall, thin, pale woman who did not appear acutely ill but showed the effect of long standing invalidism. The catheterized bladder urine contained many pus cells and on culture showed *Bacillus coli*.



Fig. 2 Case 1. Right kidney illustrating marked atrophy of the parenchyma and a renal pelvis that is elongated and altered by extensive hyperplasia of lymphoid tissue.

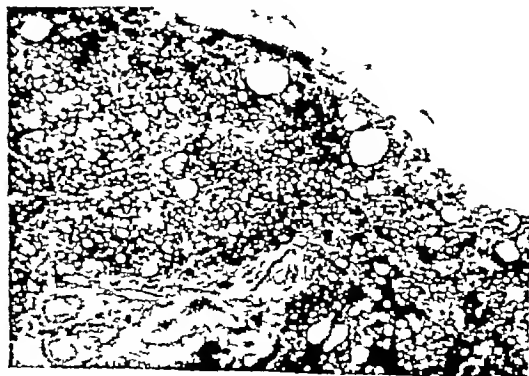


Fig. 3 Case 1. Photomicrograph through the parenchyma from the capsule to the hilus. Active glomeruli or remnants of glomeruli are not observed. Tubular spaces, most of them without a cellular lining are the only structures present.

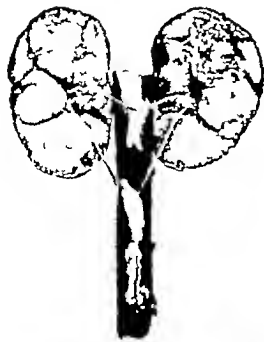


Fig. 4. Case. Urinary tract from newly born infant with large, cystic kidneys, hypoplastic ureters and renal pelvis, and epispadias.

Cystoscopic examination revealed marked hyperemia of the bladder mucosa especially in the region of the trigone. The right ureteral orifice was round and somewhat retracted, the left was normal. A catheterized specimen from the right kidney was very small in quantity (1 to 4 ccm) contained



Fig. 5. Case. A medial surface through one of the kidneys demonstrating cystic cortical tissue, disorganized renal pelvis and calyces, and medullary tissue that contains only a few large tubules.



Fig. 6. Case. Photomicrograph illustrating rudimentary mature cortex with dilated glomerular spaces, mass calyx, and the medulla in which there are only a few collecting tubules. The larger ones possessing transitional epithelium.

many pus cells and on culture showed *Bacillus coli*. Left kidney secretion was normal in amount, low cell count, and sterile. All urines are negative for bacilli, both in smears and guinea pig inoculations. There was no excretion of phenolphthalein from the right kidney and a normal amount from the left following intra-urethral injection of the dye.

The blood chemistry was normal. The blood count showed mild secondary anemia and 115,000 blood cells. The retrograde pyelogram (Fig. 7) demonstrated a rudimentary type of pelvis on the right side, the pelvis being markedly elongated, and only one small calyx was observed at the upper end. The left pyelogram was normal.

After prolonged local treatment, the patient finally consented to a right nephrectomy. The kidney as connected to find because of its small size. Extending inferiorly from it was found a long cone shaped pelvis.

**Gross pathology.** The right kidney (Fig. 8) had a maximum length of 5 centimeters, and maximum width of .5. It was shaped like a normal kidney



Fig 7 Case 3 Roentgenogram of right kidney illustrating a destructive lesion of the middle and upper calyces

except for the renal pelvis which was large in proportion to the kidney mass, and which when opened, had a pyramidal shape. There were two major calyces each being rounded and connected with the renal pelvis through an opening smaller than the greatest diameter of the calyx. The wall of the renal pelvis and calyces was thrown into convoluted parallel folds 2 to 3 millimeters wide, pigmented brown and their lining smooth. No distinct medullary pyramids were observed the entire mass of renal parenchyma being formed of light brown tissue, 4 to 5 millimeters wide. There were no striations like those of the normal medulla and cortex. The capsule was tightly adherent. There were no significant changes in the renal artery or vein.

The histological characteristics (Fig 3) center about tubular spaces that occupy all of the parenchymal mass. Most of them are round, vary slightly in size, and the lumina of most are occupied by hyaline masses. These spaces have thin walls, lining cells not being present in the majority of tubules. In sections made from the upper to the lower pole, no structures are found that represent active or obliterated glomeruli. These tubules extend to the calyces.

In this kidney the ureter, renal pelvis, and major calyces are developed to a size that is almost that of the normal kidney. In the kidney substance, only tubular structures are found. The essential derivatives of the metanephric mass, namely glomeruli, are not present. Usually when acquired lesions produce atrophy, remnants of the glomeruli are found. The conclusion reached concerning the pathogenesis of this kidney postulates that hypoplasia or aplasia of the metanephric mass occurred, whereas the derivatives of the pri-



Fig 8 Case 3 Right kidney illustrating a cyst at the upper pole dilatation of the superior calyx and cysts in the medullary pyramids of the superior pole

mary excretory duct continued well on to mature development. The hyperplastic lymphoid tissue in the lining of the renal pelvis is probably related to chronic pyelitis.

**CASE 2** This urinary tract (Fig 4) was found in a full term male child that lived 1 hour. There were two large, boggy kidneys, with irregularly developed fetal lobation markings, a short thin ureter on each side and the hilus displaced to the posterior surface of each kidney. In addition, there was a diminutive urinary bladder and an epispadias. In a surface through each kidney (Fig 5), the outstanding changes were represented by a renal pelvis the circumference of which was no greater than that of the ureter, by two short calyces also of diminutive size, by medullary pyramids in which there was only edematous tissue with a few large tubules in them. The cortical portion of the kidney was swollen, wet and made up of numerous pinpoint to pinhead size cysts. There were three irregularly formed columns of Bertini.

Histologically, the cortex was characterized (Fig 6) by dilated glomerular spaces, the glomerular tufts being approximately the size of those of a full term infant. These dilated glomerular spaces and convoluted tubules were separated by edematous stroma. A section through both cortex and medulla demonstrated a medulla in which there were only a few tubules, some of which had transitional epithelium like that of the renal pelvis instead of the normal single layer of cuboidal epithelium.

In this urinary tract, the cortical elements were developed to a fairly mature stage for a



Fig. 9. Photomicrograph of one of the medullary pyramids of the superior pole illustrating space of collecting tubules and a few large tubules and cysts lined with transitional epithelium.

newly born infant whereas in the medulla there are only isolated immature collecting tubules. The explanation of the gross and microscopic characteristics is based on hypoplasia of all of the elements that are derived from primary excretory duct, namely part of the bladder, ureters, renal pelvis, and collecting tubules, whereas the derivatives of the metanephric mass developed in a normal manner. The dilation of the glomerular spaces and convoluted tubules was due to an inadequate number of collecting tubules for excretion. The presence of epispadias is not connected directly with the malformation of the primary excretory duct, but is a concomitant malformation.

**CASE 3.** This patient, physician, aged 37 years, noticed blood in his urine. A cystoscopic examination was made the same day and blood was noted coming from the right ureter. There was some pain in the right flank following retrograde pyelogram, but this disappeared in a few days. Other than this,

the patient did not have any signs or symptoms directed to the urinary tract.

On admission to the hospital the cystoscopic examination failed to reveal any changes in the bladder except some reddening of the ureteral orifices resulting from previous catheterization.

Sterile urines were obtained from both right kidney and bladder and a study for tuberculosis was negative.

A retrograde pyelogram of right kidney (Fig. 7) showed kidney opposite the second lumbar vertebra. Pelvis was of normal size. There appeared to be destruction of the middle and upper calyces extending beyond their limits into the kidney substance.

In view of the presence of hematuria and because of the changes seen in the pyelogram, the patient, being a medical man, came to the conclusion that he had renal neoplasm and therefore requested that the kidney be removed.

**Gross pathology.** The alterations in this kidney (Fig. 8) are limited to the superior pole. There is a cyst 3 centimeters in diameter with a wall to 3 millimeters thick, the lining composed of granular, gritty material. In addition, the medullary pyramids of the superior major calyx are changed by cysts of various sizes. Under the largest of these cysts, there are noticeable depressions in the surface of the kidney which are caused by trophy of the cortex.

These alterations histologically at the upper pole (Fig. 9) are characterized by the presence of only a few collecting tubules; the medullary pyramids, some of which are dilated. The most important characteristic is the presence of a lining made up of transitional epithelium like that of the renal pelvis. Surrounding some of the tubules, there is lymphocytic infiltration. In the lining of the superior calyx there were several large hemorrhages.

The explanation of the pathogenesis of these cysts rests on retardation in the development of the later generations of collecting tubules. There was a failure also of the usual unification of the collecting tubules of the third to the fifth generations. It seems more reasonable to explain the presence of a few tubules and transitional epithelium within the medullary pyramids on the basis of retarded development rather than on metaplasia and atrophy. The failure on the part of the collecting tubules to join properly with the renal pelvis undoubtedly accounts for the dilation and formation of cysts.

In former years there was a general tendency to explain cystic malformations of the kidneys on the basis of inflammation and subsequent occlusion of ducts. At the present

time there is more frequent reference to developmental error as the probable etiological factor in the causation of cysts

#### SUMMARY

The clinical alterations and the pathological characteristics are presented of three forms of renal change that are interpreted as resulting from hypoplasia or aplasia of specific portions of the early third kidney

Histological characteristics are emphasized which seem to be standards that may be used

in deciphering rudimentary kidneys resulting from retarded development of the derivatives of the primary excretory duct or of the metanephric mass

The desirability of simplifying the terminology, until more exacting histological and embryological characteristics are established, is expressed

#### REFERENCES

1. BALLOWITZ Arch f path anat, 1895 141 309
2. BLASUS Observ Med 4 Obs 3 p 49 1677
3. PARIS Fencycl franç d'urolog, 1914, 3 230



## GENERALIZED HYPERTROPHIC PULMONARY OSTEOARTHROPATHY

AN EXPERIMENTAL AND CLINICAL STUDY WITH REPORT OF TWO CASES

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**C**LUBBING of the fingers, swelling of the joints, and periosteal new bone formation secondary to intrathoracic lesions such as bronchiectasis, empyema, lung abscess, bronchogenic carcinoma, tumor metastases to the lungs, described as pulmonary osteoarthropathy or generalized osteophytosis, is a well recognized clinical entity. Theories of the factors responsible for the new bone formation have varied from that of toxic absorption from focal infections in the chest to changes in the acidbase equilibrium through decreased aeration as a result of compression of the pulmonary blood vessels, constriction

of the bronchi or of lung compression and collapse.

Attempts to produce in experimental animals, the periosteal new bone which is characteristic of this clinical syndrome, have been uniformly unsuccessful. A preliminary report of our study of the etiological factors in the production of these bone changes was published in 1931.

The following case reports demonstrate some of the different types of intrathoracic lesions which may be associated with the production of clubbed fingers and of this new periosteal bone. Detailed pathological studies were made of the bones obtained at autopsy in the 2 cases described.



Fig. 1.—The tumor tract with an opening through the sternum has been injected. The opaque substance is seen to extend both upward and downward into cavities in the right side of the chest. The air containing tumor in this portion of the chest is obscured by either an effusion or consolidation in the lower. (Autopsy specimen of the left chest is also diagnosed from this roentgenogram.)

**CASE 1.** De S. male, aged 26 years, entered the University of Chicago Clinic May 1928, complaining of skin eruptions on the neck, upper chest, and left arm, of 9 years duration. Clubbing of the fingers was first noted about 5 weeks before coming to the clinic, and he complained of weakness, shortness of breath, loss of appetite, palpitation, and swelling of the ankles. Examination of the lesions over the chest revealed a sinus in the sternum from which pus could be expressed. There were a few scales in the chest posteriorly. Blood cytology and serology were normal. X-ray examination showed erosion and partial destruction of the left clavicle and beginning involvement of the left scapula. Blastomycetes were found in the pus. Following treatment with sodium iodide, there was improvement in the skin lesions, but the sinus continued to drain profusely and there was daily rise in temperature from 99.5 to 102 degrees. Pain in the abdomen and difficulty in breathing continued to be the outstanding symptoms and there was pitting edema over the lateral chest all. On June 26, 1928, a diagnosis of massive empyema of the right chest was made. The white blood cell count at this time was 38,400. One thousand five hundred cubic centimeters of cloudy yellow fluid were removed from the chest and hemolytic streptococci were cultured from this. Roentgenograms of the chest following lipiodol injection of the sinus, October 17, 1928, showed extensive involvement of the right side of the thorax (Fig. 1).

Roentgenograms of July 3, 1928 showed periosteal new bone formation along the shaft of the

radius and ulna and of the tibia and fibula and this became more marked at each succeeding examination (Fig 2). Chronic empyema persisted. The patient was discharged from the hospital October 31, 1928, and re-entered March 7, 1929. He had been confined to his bed during the interval of 5 months. The skin lesions had healed leaving dense scars, but the draining sinus in the sternum was still present. Blood chemistry studies were made at intervals from March 9, 1929, to March 21, 1929, the day before death occurred, and these showed blood calcium from 7.0 to 8.5 milligrams per cent, figures which are at least 20 per cent below normal for an adult, and inorganic phosphates of 3.69 to 4.42 milligrams per cent, slightly higher than the normal adult average (Table I). There was a slight increase in the carbon dioxide content from 66.9 per cent to 71.16 per cent and a corresponding shift of the hydrogen ion concentration toward the acid phase from an initial reading of 7.62 (definitely more alkaline than normal) to 7.49. During the period of this blood study, the patient was dyspneic but there was no hyperpnea and the changes from normal

indicate that there was inadequate aeration of the blood and hence accumulation of carbon dioxide in the tissues in spite of the fact that the patient was kept at rest. This lack of adequate oxygen intake and accumulation of acid products in the blood and tissues has been suggested as the etiological factor in the production of the bone changes. Renal function was not seriously impaired and the non protein nitrogen, urea nitrogen, and blood chlorides were normal, rising only slightly on the day preceding death, March 21, 1929.

*Autopsy.* There was relatively little normal lung tissue containing air and the right lung was almost entirely destroyed by the long standing infection. The long bones were thickened. One tibia, fibula, and ulna were removed for study. X-rays of these bones revealed periosteal new bone formation entirely surrounding the shafts of the bones but absent at the ends of the shafts where there is known to be no periosteum. When these bones were cut longitudinally, the new bone was found to be from 1 to 5 millimeters in thickness and possessed a thin cortex with new cancellous bone filling in the space between

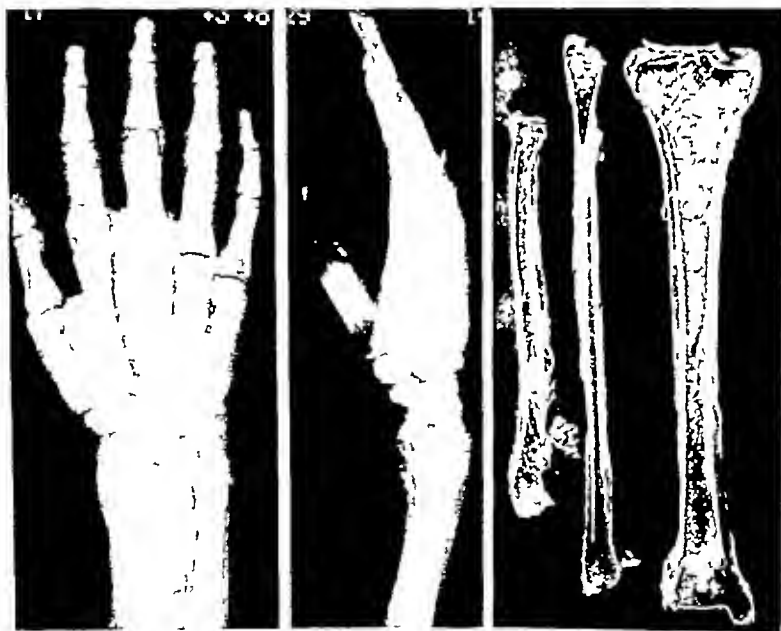


Fig 2

Fig 3

Fig 2, left. Case 1. There is marked periosteal new bone formation about radius and ulna and an appearance of increasing density or sclerosis in the shafts of these two bones. This periosteal new bone formation is noted also on all of the metacarpal bones and bones of the proximal phalanges. No bony changes are noted in the distal phalanges.

Fig 3. Case 1. Photograph of the surfaces made by sectioning the tibia and fibula and ulna longitudinally shows a wide zone of periosteal new bone formation particularly on the medial side of the distal two-thirds and on the lateral side of the proximal two-thirds of the tibia and fibula and ulna with less new bone formation in the middle thirds and none at all adjacent to the articular surfaces.



Fig. 4. Case. Photomicrograph of section of the distal end of the tibia. A, left. The outer portion of this new bone is slightly denser than that near the old cortex and denser than new cortex in forearm. There is some smooth absorption of the old cortex on both the medullary and

the outer surface with areas showing induration and an occasional giant cell and bony absorption. There are very few cells of any kind and no infiltration of round cells. The type of the new bone which has formed is that which is usually seen in the site of an injury to bone. B, A higher power shows both absorption of the bone trabeculae throughout the cancellous portion of the old shaft and definite new bone formation. The extra-cortical new bone has been formed in irregular trabeculae and the spongy bone is highly vascular particularly just outside the old cortex.

this and the old cortex which was still intact. The cortical and cancellous portions of the old shafts were grossly normal (Fig. 3). Macroscopic sections of the tibia and fibula show the raised periosteum and the space between periosteum and the old cortex is filled with spongy cancellous bone which has surrounded the shaft increasing its diameter by 5 to 50 per cent. There is slight absorption of the old cortex. The legends for Figures 4 and 5 describe the macroscopic pathology.

This is the first case of which we have knowledge in which pulmonary osteomyelitis has been demonstrated to be secondary to blastomycosis infection. In this case there was secondary infection from *Streptococcus hemolyticus* and the development of massive empyema with marked and prolonged respiratory embarrassment. The increase in carbon dioxide content and the gradual shift from a very alkaline hydrogen-ion concentration to one more nearly normal near the terminal stages of the disease adds some support to the theory that the bone changes which are characteristic of pulmonary osteomyelitis may be due, in part at least, to a decrease in the oxygen available to the tissues and an increase in the carbon dioxide content. The presence

of massive and prolonged chest infection is an argument in favor of the theory of toxic absorption as the primary etiological factor.

**CASE.** J. B., aged 50, white male, entered the University of Chicago Clinics January 5, 1917, complaining of a lump on the right side of the neck of 3 years' duration and of additional swellings in the neck which had appeared more recently associated with a yellowish discharge from the nose and nasal discharge from a sinus in the site of the swelling in the neck. He had lost 50 pounds in weight and was weak and emaciated. He complained of dysphagia and dyspnea. Bloody material was expectorated from time to time.

Examination showed several distinct hard masses from 1 to 2 centimeters in diameter on the right side of the neck and small mass in the left axilla. His fingers were clubbed and the skin was slightly cyanotic. The right side of the pharynx was distorted by the bulging of the mass and the right tonsil was pushed forward.

Blood serology was normal. White blood cells, 2,400; red blood cells, 5,000,000 and the urine contained hyaline casts and plus albumin.

An X-ray of the chest showed large pleural mass in the region of the left axilla with erosion of the ribs and an enlarged aorta (Fig. 6). Further X-ray pictures revealed well marked pulmonary osteomyelitis of the forearms (Fig. 7) and legs. These findings, together with the study of section of

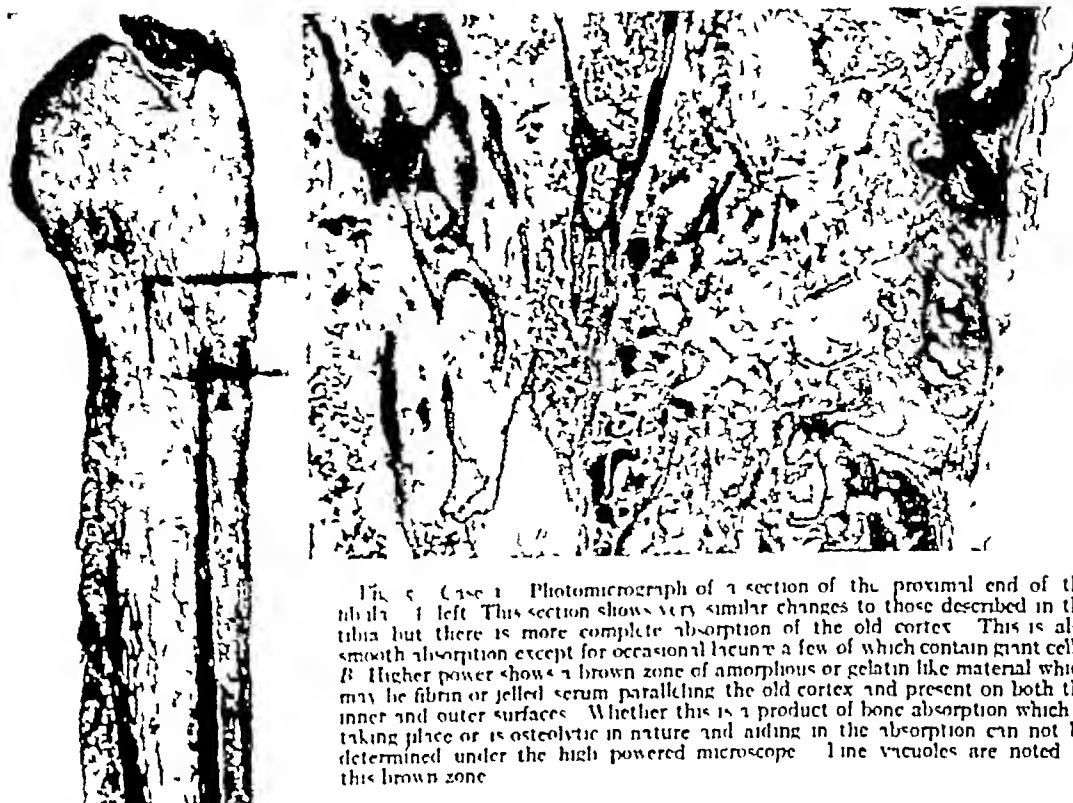


FIG. 5. Case 1. Photomicrograph of a section of the proximal end of the tibia. A. Left. This section shows very similar changes to those described in the tibia but there is more complete absorption of the old cortex. This is also smooth absorption except for occasional lacunae a few of which contain giant cells. B. Higher power shows a brown zone of amorphous or gelatin like material which may be fibrin or jelled serum paralleling the old cortex and present on both the inner and outer surfaces. Whether this is a product of bone absorption which is taking place or is osteolytic in nature and aiding in the absorption can not be determined under the high powered microscope. Fine vacuoles are noted in this brown zone.

tissue removed at biopsy from the mass in the neck, led to a diagnosis of carcinoma with probable metastases to the mediastinum, ribs, axilla, and the brain stem and secondary pulmonary osteophytosis.

Blood chemistry studies were made (Table II). Changes from normal were similar to those noted in Case 1. Blood calcium was 6.75 and inorganic phosphates were 5.70. The carbon dioxide content was definitely increased to 67.0 and the hydrogen ion concentration was alkaline 7.61. The basal metabolic rate was +42 but since the body temperature was 100 to 101 degrees, this was discounted. Respirations averaged 30 per minute and during the

last 2 days these increased to 40 per minute. Bronchopneumonia developed and all day February 5, 1920 until his death at 4:00 p.m. there was marked dyspnea and cyanosis. A terminal decrease in the carbon dioxide content and the shift of the hydrogen ion concentration toward normal may have been due to the increased respiratory rate but the persisting cyanosis and dyspnea indicated that there was not a corresponding increase in oxygen that was reaching peripheral tissues.

**Autopsy.** Examination revealed a primary carcinoma of the nasopharynx with metastases to the neck, axilla, mediastinum, lungs, liver, brain, ribs,

TABLE I

Case 1. I. DeS. No. 4063. Age 27 years. Bile tomecosis and pulmonary osteoarthropathy

Date	Ca	P	CO <sub>2</sub>	pH	Remarks
3-9-20	7.9	3.69	66.9	7.62	Blood 3 hours after lunch
3-11-20	7.7	3.84	66.01	7.56	Before breakfast. NPN 24 urea N 7 Cl <sub>2</sub> 50.1
3-12-20	8.5	4.32	69.8	7.53	Before breakfast
3-13-20	8.5	4.42	71.16	7.49	Before breakfast. Intrav. No iodides given yesterday
3-18-20					NPN 29 urea N 13 chlorides 462.4
3-21-20					NPN 41 urea N 24



Fig. 6. Case. This X-ray picture of the chest of Case was taken 5 weeks before death. There is shadow of the lobes of the lung but the peripheral lung tissue does not seem to be involved. (This appearance of minimal involvement of the lung was confirmed at autopsy.) There is no obvious enlargement of the heart. This minimal cardio-respiratory pathology makes it more difficult for us to explain the dyspnea and osteoarthropathy which were present.

and the vertebrae. The bones of the forearm were removed and roentgenograms of the radii and ulnae revealed extracortical or periosteal new bone formation (Fig. 8). When the bones were split longitudinally the surfaces made by cutting the newly formed bone were similar to those described in Case 1. Microscopic sections were studied and these revealed new cancellous bone forming outside of the old cortex. The periosteum was raised and the spongy cancellous bone was similar to that found in the medullary portion of the old bone. A thin cortex was noted just beneath the raised periosteum. The cortex of the old bone was undergoing both smooth and, to a lesser extent, lacunar absorption. The changes were almost identical with those described in sections from the tibia and fibula of Case 1.

Although there was a small sinus at the site of the carcinomatous mass in the neck of this patient the evidence of secondary infection was negligible. There was no empyema or other massive or chronic intrathoracic infection. Unless one assumes a possible toxic ab-



Fig. 7. Case. X-ray film of the hand showing periosteal new bone about the distal portion of the ulna and radius and also on the first metacarpal bone. The chattering of the fingers can be seen but, as has been previously described, is confined to the soft parts and there are no definite changes noted in the bones of the distal phalanges themselves.

sorption from the carcinoma itself we have here a case of extensive pulmonary osteophytosis without basis for the theory of toxic absorption to explain it. The factors common to both Cases 1 and 2 are respiratory embarrassment due to compression of a portion of one lung and some evidence of intrathoracic circulatory disturbance from mechanical pressure.

#### HISTORICAL REVIEW

Osteoarthropathy or osteophytosis is a non-suppurative affection of the extremities of the body found secondary to disease of the lungs, heart, or liver. Bamberger first described the bone changes characteristic of this disease in 1889 and Marie in 1890 named it hypertrophic pulmonary osteoarthropathy although the most constant and striking changes produced are seen in the shafts of the long bones. Arnold suggested the name of secondary hyperplastic osteitis, but the condition has been referred to most often in the literature by the name of Bamberger Marie's disease or the rather lengthy term devised by Marie

In 1915 Locke collected 144 cases from the literature. Stephens of the Mayo Clinic, collected 156 cases in 1928 and discussed the various theories which had been suggested to explain the etiology of the disease and attempted to reproduce the condition in dogs.

A study of these papers indicates the extensive changes which may occur in various tissues of the body secondary to chronic diseases of the lungs, heart or, rarely, of the liver. The tissues affected include the skin and its appendages, the subcutaneous tissue, the joints, muscles, and the bones. *Clubbing of the fingers* is due to thickening of the soft tissue, for no bone change in the distal phalanx has been described, due possibly to the fact that this terminal digit has no periosteal covering. This change in the fingers is often associated with hypertrophy of the nails, the sweat glands, and pigmentation of the skin, and the nose may also be enlarged. *Joints* may be swollen and painful due to swelling of the synovia associated with a round cell infiltration and later erosion of articular surfaces. These changes may lead to limitation of motion and deformities, the most common being curvature of the spine. The latter deformity may be explained in most cases on a basis of the mechanical disturbance due to unilateral or bilateral disease of lung or pleura and is as often present without manifestations of osteoarthropathy as with it. *Muscle atrophy* and generalized weakness are probably secondary to the joint involvement and the debilitating effect of the disease and not to primary injury to the muscles themselves. *Bone changes* are striking and have been of most interest in the study of this disease. These consist of symmetrical proliferative periostitis, first involving the lower third of



Fig 8 Case 2 Bones of the forearm which were removed at autopsy and have been stripped of most of the soft tissue attachments. Periosteal new bone has formed particularly on the posterior surface of the ulna in its proximal and distal thirds. There is some evidence of beginning absorption of the outer portion of the cortex of the ulna and a thin but definite new cortical zone forming on the outer portion of the periosteal new bone. Less evidence of new bone formation is noted in the radius but it is more evenly distributed along the shaft of the bone and throughout its length. In the case of the ulna, there is some lamination or onion peel appearance to the new bone that is formed, which is similar to that which is sometimes seen at the site of a Ewing type of undifferentiated round cell sarcoma.

the diaphyses of the tibia, fibula, radius, ulna, the metacarpal and the metatarsal bones, and later the more proximal portions of the shafts

TABLE II

Case 2 J. B. No. 9164 Age 50 years Pulmonary osteoarthropathy					
Date	Ca	P	CO <sub>2</sub>	pH	Remarks
2-1-29	6.75	5.29	67.0	7.615	Blood before breakfast Patient's respiratory distress not marked today
2-2-29	7.74	9.52	69.9	7.48	1½ hrs. after breakfast
2-4-29	8.59	6.33	67.9	7.36	Marked respiratory distress Rapid respiration and gurgle in throat
2-5-29	Ins	q—		7.355	9 a.m. Breathing stertorous
2-5-29	7.84	5.52	64.3	7.35	Chlorides 543.2 1½ hrs. before death Resp 60 Skin pale and clammy



Fig. 9. Dog 8. Shows complete collapse of the right hind permitting 7 months after the injection of 200 cubic centimeters of paraffin into the chest.

of the leg and arm bones. In advanced stages of the disease, the clavicle, the spines of the scapula and the vertebrae may be involved. Increase in length of the long bones has been reported.

#### MICROSCOPIC PATHOLOGY

The changes noted in the microscopic sections of the two cases which we have studied and described were well advanced. Stephens has described the early appearance of new bone formation in this disease. In its early state the new bone consists of thin layers which form immediately below the periosteum and, as the condition progresses the layer on layer around the bone. These layers tend to be heavier on the lateral than on the medial sides of the shafts, and heavier on the fibula than on the tibia and are equally deposited on the radius and ulna. At first the layers of periosteal bone are distinctly separate from each other they may accumulate until as many as six or more layers are present and distinguishable in the roentgenograms. In this stage the new bone is soft very friable

and easily cut, or readily torn from the underlying cortex. It is very vascular and in performing a biopsy on a fibula a packing of gauze was necessary to control hemorrhage in one of the cases studied at the Mayo Clinic. In the advanced stage the new bone is firm but continues to present a picture of a second bone surrounding the old shaft with its zone of firm cancellous bone bounded by a thin, but hard, cortex under the raised periosteum. There are no longer distinct layers and the cancellous bone is irregular but still very vascular. The old shaft retains its form but is less dense due to loss of lime salts and an increase in fat content. Shafts are increased in diameter and circumference.

#### ETIOLOGY

Pulmonary osteoarthropathy has occurred most commonly in young patients. Among the conditions which have been shown to be primary in the production of the peripheral changes which make up this syndrome may be listed (1) tuberculosis of the lungs with cavities (2) bronchiectasis (3) empyema (4) pneumonia (5) pleurisy (6) syphilis (7) chronic valvular disease of the heart, especially when associated with passive venous congestion (8) malignant tumors, such as carcinoma or sarcoma of the lungs (9) and local circulatory conditions, such as aneurism, which may produce venous congestion. Other conditions described as primary but which cannot be accepted as etiological factors without further evidence to support the contention include (1) pyelonephrosis (2) dysentery (3) influenza (uncomplicated) (4) chronic jaundice (5) alcoholism.

The following theories have been advanced to explain the changes noted in hypertrophic pulmonary osteoarthropathy.

1 Marie Bamberger and Symes-Thompson thought that a toxin was produced probably by bacterial decomposition, and absorbed into the blood stream to produce the changes in the tissues characteristic of the disease.

2 Thayer considered it part of the picture of amyloid degeneration.

3 Masalongo believed that it occurred only in cases of arthritic diathesis and in this he was supported by Symes-Thompson.



Fig 10 Dog 795 Roentgenogram of chest 8 months after collapse of the left lung and subsequent removal of the lower and accessory lobes of the right lung

4 Thorburn called attention to the striking similarity between the periosteal new bone in osteoarthropathy and that which may be seen along the shafts of bones adjacent to tuberculous joints. He pointed out that postmortem examinations frequently confirmed the diagnosis of tuberculosis in patients showing these peripheral changes when tuberculosis had not been found in the course of clinical examinations, and, on a basis of these findings, he advanced the theory that all cases of osteoarthropathy were a form of tuberculosis which affected principally the long bones and the joints.

5 Berent suggested that the syndrome was due to a nerve disease and compared it to changes which are sometimes noted in syringomyelia.

6 Davis, Brooks, Kessel, Hyman and Herick, Bryan, and Stephens have offered arguments and some evidence to support the theory that the changes in osteoarthropathy may be explained entirely on a mechanical factor of blood stasis. Campbell states "Clubbing (of the fingers) is the result of defective



Fig 11 Roentgenogram of dog's chest taken 3 weeks after direct inoculation of each of the right upper, middle, and lower lung lobes, through a thoracotomy opening, with 0.2 cubic centimeter of a heavy suspension of human tubercle bacilli (H119) in lipiodol. The right upper lobe bronchus was completely stenosed a few days before the picture was taken and the right upper lobe is completely atelectatic. The right middle and lower lobes each exhibit a large irregular thick walled abscess. The animal was sacrificed 5½ months later. At no time were there peripheral or X ray evidences of generalized osteophytosis.

oxidation in the tissues of the extremities, whether produced mechanically by obstruction to venous return, or as the result of a general lowering of the oxygen tension of the blood affecting parts of the body where normally the circulation is slow."

7 Bryan, Kleinberg, Marcus, and Phemister have expressed the opinion that at least two factors were necessary to produce hypertrophic pulmonary osteoarthropathy. First, a toxemia from a long standing disease in the chest and, second, circulatory disturbances resulting from either cardiac or pulmonary involvement.

8 Harter thought that the condition was due to lack of oxygen and called attention to the somewhat similar changes found in some people living in high altitudes where oxygen is rare.



TABLE III.—RESULTS OF INJECTING PARAFFIN INTO PLEURAL CAVITY

This table shows blood chemistry studies of the three dogs surviving for the longest period. There were no consistent changes in the acid base balance or the calcium and inorganic phosphate content of the serum.

Dog No.	Date	Days since onset	Blood serum chemistry						Comment
			(CO <sub>2</sub> )	pH	Ca	P	Ca	P	
21	7-29-29		20	7.4	12	5	46		Normal—fasting
	7-30			7.3	7		30.5		Normal—fasting
	7-31-29		20	5					100 cc. paraffin injected into right pleural cavity
	8-7-29		20			5	5		Normal—no dyspnea
	8-11-29	22	21	7	5		21		No arthropathy
	8-1	200	20.9			5	42		7-27-29 Right chest flat to percussion. X-ray shows no air in right chest, but no evidence of paraffin in bone
	8-4-29	201	43	7	30	5	27		No arthropathy
120	7-29-29		23	7		5	22		Normal
	7-30			6	6	5	66		Normal
	7-31-29		20.7						100 cc. paraffin injected into right pleural cavity
	8-3-29	5	23	7.3			27		Labored breathing
	8-10-29	17	42			5.9	47		Hematuria of blood
	7-14-29	16			30		24		No arthropathy
	8-18	28	29.6				29		
	8-23	33	25.6				22		7-27-29 No arthropathy. X-ray tells us in chest
	8-28-29	38	43				26		
33	8-2-29				20.5	5	24		120 cc. paraffin, right chest
	8-30	28	34	5		6			8-6-29 No changes at lower end of tibia or fibula
	8-30	28	20	5		6	29		7-27-29 X-ray shows no bone changes. Chest looks clear
	8-30	28	20			6	24.5		

\*M.grams per each 100 cc.

P shows per cent carbon dioxide content

#### EXPERIMENTAL STUDIES

Attempts to produce in experimental animals changes characteristic of the clinical syndrome of hypertrophic osteoarthropathy have been uniformly unsuccessful.

Bamberger, believing a toxin to be the cause of the bone changes, injected into the rectum of 3 young rabbits twice daily a bronchoectatic secretion secured from 1 of his patients, but did not produce any of the changes.

Pfeister injected cultures of various organisms including *Streptococcus viridans* and *Streptococcus hemolyticus* into rabbits for a period of 6 weeks without producing any bone changes.

Stephens tried to support his theory that all of the changes noted could be explained on a basis of peripheral blood stasis. He produced mechanical interference with the venous flow of blood in dogs creating venous con-

gestion in the extremities, but was not successful in producing a proliferative periostitis.

Harter and Churchill sought to produce the changes by ligating and sectioning the bronchus in cats and monkeys and in other ways tried to create a lowered oxygen content in the peripheral blood, but they were not successful in producing any changes in the bones, nails or capillaries of the nail beds.

We attempted to produce the syndrome of hypertrophic pulmonary osteoarthropathy in dogs by creating intrathoracic complications which are similar to those which in the human being have been found to predispose to the development of clubbed fingers and periosteal new bone formation.

Roentgenograms were made of the bones of the extremities both before and at intervals after the operations on the chest and the calcium and inorganic phosphate and carbon

TABLE IV—RESULTS OF COLLAPSE OF LUNG BY STENOSIS OF BRONCHUS

Dog No.	Date	Days from first	Blood serum chemistry					Comment
			CO <sub>2</sub>	pH	Ca	P	Ca x P	
64	7-12-37				10.8	4.5	48.5	7-12-37 Stenosis begun
								8-10 Complete stenosis
	9-10-37	61		7.6	10.1	5.0	50.0	11-10-37 No arthropathy
	11-10-37	115	45.4	7.5	11.3	8	91.4	
	2-14-38	213	45.0	7.2	10.2	7.9	80.0	2-14-38 Negative X rays
400	5-13-38	156	45	7.4	11.0	4.2	46.3	No new bone formation
	5-27-38			7.6	12.1			100% AgNO <sub>3</sub> to stenosis accessory and right mid bronchi
	4-10-39	11	43.4		10.0	4.0	40.0	Stenosis Rt lower lobe bronchus cauterized 6-10-39 end is complete to right
	7-2-39	105	43.4		10.2	5.5	56.3	
	9-10-39	15		7.5	10.6	4.5	47.0	
80	11-10-39	33	48.4	7.5	11.0	4.0	44.0	11-1-39 X rays show no periosteal change
	1-4-38	334	45.5	7	10.8	2.5	27.0	1-4-38 No lamellar bone change
	3-7-38	343	48.0	7.2	10.5	4.0	42.0	No periosteal new bone
	7-12-37				10.5	4.8	50.0	Stenosis (right bronchus) begun 7-12-37
	9-10-37	63		7.5	10.8	5.3	56.0	9-10-37 Total collapse and curetlet removed 11-5-38 X rays show arthropathy
95	11-10-39	115	4.5	7.5	11.4	5.4	61.6	
	2-14-38	184	45.1	7.2	10.5	5.0	52.5	2-14-38 X rays negative
	5-11-38	79	45.1	7.4	11.5	4.4	50.7	No osteoarthropathy
	7-12-37							X rays—very little air in lung No osteoarthropathy
	3-2-38	8	45.6	7.2	10.5	5.5	57.0	Collapsed left lung right lower and accessory removed
	5-13-38	9	51.8	7.5	11.7	5.8	68.4	No osteoarthropathy

Milligrams for each 100 c.c.m. No urea per cent carbon dioxide content.

dioxide content and the hydrogen-ion concentration of the blood serum were determined.

Of 9 dogs into whose right pleural cavity from 100 to 300 cubic centimeters of paraffin was injected, 1 survived 9 months and 2 were sacrificed after 18 months. In each instance, in addition to the mechanical pressure on the lung by the paraffin there was a prompt pleural effusion which almost completely compressed the lung in the right half of the chest, and displaced the heart and the mediastinum to the left, reducing the air space in the left side of the chest (Fig. 9). No consistent or significant blood changes were noted following the injection of the paraffin (Table III). No periosteal new bone formation or other changes characteristic of osteoarthropathy were observed.

By means of a method described by one of us, collapse of one or more lobes of the lungs of 13 dogs was accomplished. One of the dogs developed a lung abscess, and lobectomy was

performed upon 5 dogs at varying intervals following collapse of the lobe or of the corresponding lung. Roentgenograms of the chest of each dog showed the diminished air containing lung tissue. Figure 10 is the X-ray of the chest of a dog following collapse of the left lung after stenosis of the bronchus by means of silver nitrate cauterization and subsequent removal of the right lower and accessory lobes. Only the right upper and middle lobes of the lung contain air and yet this dog was not dyspneic and no osteoarthropathy developed. The animals in this series were exercised vigorously each day for several weeks by being forced to swim in a tank, but in spite of this forced exertion which did produce temporary dyspnea there were no significant changes in the blood chemistry determinations. The results of four of these studies are included in Table IV. As will be noted from this table, for a few days to a few weeks after the functioning lung tissue had

been reduced to a minimum there was a definite change in the hydrogen ion to the acid side of normal. These dogs seemed to be able to adjust themselves to the change very quickly for the hydrogen ion concentration returned to normal and temporary signs of respiratory embarrassment disappeared.

Twenty-eight dogs were successfully inoculated with tubercle bacilli and abscesses produced in the lung in each instance (Fig. 11) and empyema in the chest in one dog but in no instance were we successful in producing any of the peripheral or bone changes which are characteristic of the clinical syndrome of hypertrophic pulmonary osteoarthropathy.

#### EVALUATION OF STUDY

The clinical syndrome known as secondary hypertrophic pulmonary osteoarthropathy usually develops in association with chronic intrathoracic disease. The most common primary diseases leading to the changes characterized by clubbing of the fingers and periosteal new bone formation along the shafts of the radius and ulna, fibula and tibia and less often the metacarpal or metatarsal bones are bronchiectasis, empyema, and tuberculous with cavities in the lung. There is usually definite evidence of both circulatory and respiratory embarrassment including dyspnea, venous congestion and cyanosis in the distal portion of the extremities. The concomitant occurrence of infection and usually of suppuration in the thorax has led to the theory that absorbed toxins were at least in part responsible for the more peripheral changes in the bones and soft tissues. Report of cases with well advanced hypertrophic osteoarthropathy secondary to malignant growths such as sarcoma or carcinoma of the lung without abscess formation or other chronic infections discredits the toxin theory. The only constant finding is that of disturbed circulation and in most cases, dyspnea as well as cyanosis. We not only failed to produce the osteoarthropathy in experimental animal but were unable to bring about prolonged dyspnea or cyanosis or changes in the acid base equilibrium. In the cases which we have studied there was an increase in the carbon dioxide content of the serum and except toward the terminal stages

of the disease a change in the hydrogen-ion concentration toward the alkaline side. After a review of other theories and of the findings in the cases which we have studied we are inclined to support the theory that these changes noted in our cases were due to decrease in the oxygen content of the serum and may have been due to a corresponding increase in waste products of a metabolic nature. The report of clubbing of the fingers and of periosteal new bone formation in individuals who have no known intrathoracic complications, but who live at high altitudes where the air is rarefied, supports this hypothesis.

We have tried without success to produce hypertrophic pulmonary osteoarthropathy: (1) by pressure upon a lung from a foreign body in the pleural cavity (2) atelectasis of a primary or secondary bronchus (3) collapse or total absence of a lobe or of an entire lung (4) pleurisy with effusion (5) empyema and solitary lung abscess. In the human subject any of the above intrathoracic complications might be expected to produce respiratory embarrassment with varying degrees of dyspnea, cyanosis, and venous engorgement in the tissues most distant from the heart. None of these changes were noted in the experimental animal which seemed to be able to compensate for loss of functioning lung to a surprising degree even when forced to vigorous exercises such as continuous swimming for an hour or longer.

Gollee has reported complete recovery of an advanced case of hypertrophic pulmonary osteoarthropathy after healing of an empyema cavity following removal of a piece of rubber drain that had been retained there for several years.

#### SUMMARY

1. Hypertrophic pulmonary osteoarthropathy is usually secondary to intrathoracic disease.
2. Such diseases are usually of long standing before the changes in the extremities are noted.
3. Infection or suppuration is not essential to the production of osteoarthropathy.
4. Two cases are reported: one of blastomycosis of the chest wall with secondary infection and empyema and a second of

carcinoma of the lung with involvement of the bronchi and larger blood vessels but no intrathoracic suppuration. The conditions common to both cases were dyspnea and cyanosis and a disturbance of the acid base equilibrium of the peripheral blood.

5. Intrathoracic complications were created in dogs but we were unable to produce dyspnea or cyanosis, and blood chemistry studies showed no consistent or sustained variation from normal. Although chronic abscess and empyema were produced in the chest of some of the dogs, there was no suggestion of clubbing of the phalanges, edema or periosteal new bone formation in any of these animals and the animals quickly recovered from dyspnea which was brought on by strenuous exercise.

6. The bones of the extremities of 2 clinical cases of hypertrophic pulmonary osteophytosis which were examined at autopsy were studied both grossly, by X-ray and microscopically. These showed a chronic proliferative osteitis with a shell of new cancellous bone 1 mm to 5 mm thick completely surrounding the tibia, fibula, radius and ulna. A thin new cortex was present just beneath the raised periosteum.

7. No conclusions can be drawn from this series of cases or from the negative results obtained in our experimental studies, but we are led to add our opinion that the secondary changes of osteoarthropathy are not due to a toxin but can be explained on the mechanical basis of blood stasis or of poor aeration of the blood creating changes in the acid base equilibrium.

# BIBLIOGRAPHY

1. ADAMS, W. E. Safe and reliable method for closing large bronchi. *J Thor Surg*, 1933, 3, 198.
2. ADAMS, W. E., and LIVINGSTONE, H. M. *Ann. Surg.*, 1932, 95, 106.
3. Idem. Lobectomy and pneumectomy in dogs. *Arch. Surg.*, 1932, 25, 898.
4. ADAMS, W. E., and VOZIWALD, A. J. The treatment of pulmonary tuberculosis by bronchial occlusion. *J Thor Surg.*, 1934, 3, 633.
5. AELTOLD, J. Acromegalie, Pachyactrie oder Ostitis? *Beitr. z. path. Anat. u. z. allg. Path.* 1891, 10, 1.
6. BAMBERGER, E. Ueber Knochenveränderungen bei chronischen Lungen und Herzkrankheiten. *Ztschr. f. klin. Med.*, 1890, 18, 183.
7. BERENT, W. Zur Aetiologie osteoarthropathischer Veränderungen. *Berl. klin. Wochenschr.*, 1903, 40, 75.
8. BROOKS, H. A discussion of the pathogenesis of hypertrophic pulmonary osteoarthropathy, with a report of four cases. *New York M. J.*, 1911, 91, 1215, 1913, 95, 000.
9. BRANT, L. Secondary hypertrophic osteoarthropathy with metastatic sarcoma of the lung. *Am. J. Roentgenol.*, 1920, 7, 285.
10. CAMPBELL, D. The Hippocratic fingers. *Brit. M. J.*, 1914, 1, 145.
11. COMPÈRE, E. L., ADAMS, W. E., and COMPÈRE, C. L. Possible etiologic factors in the production of pulmonary osteoarthropathy. *Proc. Soc. Exper. Biol. Med.*, 1931, 28, 1083.
12. CRUMP, C. Histologie der allgemeinen Osteoporose. *Arch. f. path. Anat.*, 1909, 271, 457.
13. DAVIS, N. S. Pulmonary hypertrophic osteoarthropathy. *J. Am. M. Ass.* 1895, 21, 8-5.
14. DRASTICH, L., ADAMS, W. E., HASTINGS, A. B., and COMPÈRE, C. L. The effect of exercise on the acid-base balance and oxygen of the blood following atelectasis and pneumectomy. *J. Thor. Surg.*, 1934, 3, 341.
15. GODLEE, H. J. Bone and joint changes in connection with thoracic disease. *Brit. M. J.*, 1896, 2, 57 and 116.
16. HARTER, J. S., and CHURCHILL, E. D. Communication from the authors.
17. HYMAN, C. H., and HERRICK, T. P. Chronic osteoarthropathy. Report of a case in a child aged twenty-eight months. *J. Am. M. Ass.*, 1922, 75, 10-3.
18. KESSEL, L. The relation of hypertrophic osteoarthropathy to pulmonary tuberculosis. *Arch. Int. Med.*, 1917, 19, 239.
19. KLEINBERG, S. Secondary pulmonary hypertrophic osteoarthropathy. Report of a case. *J. Am. M. Ass.*, 1921, 70, 435.
20. LOCKE, E. A. Secondary hypertrophic osteoarthropathy and its relation to simple club-fingers. *Arch. Int. Med.*, 1915, 15, 639.
21. MARCUS, J. H. Hypertrophic pulmonary osteoarthropathy. Report of a case. *Arch. Pediat.*, 1917, 4, 38.
22. MARIE, P. De l'ostéo-arthropathie hypertrophique pneumique. *Rev. méd.*, 1890, 10, 1.
23. MASSALONGO, R., and GASPARDI, U. Sulla osteoarthropatia ipertrofica pneumica. *Polidin. Roma, sez. med.*, 1913, 20, 433.
24. MILLS, R. G., and MCKEE, N. Bronchogenic squamous cell carcinoma. *Arch. Int. Med.*, 1929, 43, 516.
25. PHEMISTER, D. B. Chronic lung abscess with pulmonary hypertrophic osteoarthropathy. *Surg. Clin., Chicago*, 1917, 1, 381.
26. STEPHENS, B. P. Secondary osteoarthropathy and its etiology. Unpublished thesis, Mayo Foundation, Rochester, Minn.
27. STILES-THOMPSON, H. Hypertrophic pulmonary osteoarthropathy. *Med.-Chir. Trans., London*, 1904, 87, 85; *Lancet*, 1904, 1, 157.
28. THAYER, W. S. Hypertrophic pulmonary osteoarthropathy and acromegaly. *New York M. J.*, 1890, 63, 35; *Philadelphia M. J.*, 1898, 2, 955.
29. THORNTON, W., and WESTMARTON, F. H. The pathology of hypertrophic pulmonary osteoarthropathy. *Tr. Path. Soc. Lond.*, 1897, 47, 177; *Re. Brit. M. J.* 1896, 2, 921.

## PREGNANCY COMPLICATING DIABETES

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**P**REVENTION of the death and decay of the over ripe fetus of the diabetic mother is a challenge today to the obstetrician and research worker in the field of diabetes. Maternal mortality attributable to the disease has been conquered in the insulin era, but stillbirths and the macerated fetus of the giant type are nearly as characteristic of diabetic pregnancies which are allowed to come to full term today as they were in the pre-insulin era.

Two hundred fifty-seven pregnancies have occurred in 180 diabetic women in the series of patients seen by Dr. Joslin from 1898 to October 10, 1934. One-half of these occurred in the pre-insulin and one-half in the insulin eras. Of this number 66 were under our immediate care. The series differs from others which have been published because it includes 22 pregnancies in 15 patients who had onset of the disease in childhood. The age at onset of the diabetes in this special group varied from 8 to 14 years, and the duration of diabetes at onset of pregnancy from 2 to 14 years. This small group is unique and we believe forewarns us of the problems of the pregnant diabetic woman of the future.

TABLE I—OUTCOME OF PREGNANCIES DELIVERED AT TERM

( ) Non-diabetic, ( ) our patients prior to onset of diabetes, ( ) in diabetes in the pre-insulin, ( ) in the insulin eras, and ( ) in diabetic patients directly under our care.

	Living births per cent.	Stillbirths per cent.
Johns Hopkins series of "all types" consecutive cases (used as control group)	94	4
Our patients prior to onset of diabetes	80	20
Pre-insulin era		29
Insulin era	79	21
Patients under our immediate care	86	

\*Fackham, C. R. Johns Hopkins Hosp., 1914, 34. 86

\*\*Undoubtedly includes early undiagnosed diabetes

**Scope of problem.** The problem of pregnancy complicating diabetes is increasing in importance. There are some 100,000 (14) diabetic women of childbearing age in the United States, and if the known pregnancy rate of our own series, which is 10 per cent, may be applied to the diabetic population at large, the problem directly concerns some 10,000 diabetic women or 1,500 annually. That diabetes does play a menacing rôle in the successful outcome of pregnancy is unquestionable. In our own series of patients, this is evident in a comparative analysis of diabetic pregnancies and pregnancies in a non-diabetic series, and also in a comparison of pregnancies in our own patients prior to and following the onset of the disease.

Although Table II shows only a slight improvement of the insulin era over the pre-insulin era in all cases, this does not indicate a failure of insulin therapy but rather its success, for the inclusion of a large series of severe diabetics of the new generation of youthful diabetics, and the long duration cases, alter comparative statistics. Some of these pregnancies could not have occurred and others would have been interrupted in the pre-insulin era.

TABLE II—COMPARISON OF PREGNANCIES IN OUR PATIENTS

( ) Prior to onset, (x) after onset in the pre-insulin and ( ) in the insulin era, and (x) under our own care.

	Living births		Stillbirths		Miscarriage at abortion	
	No.	Per cent.	No.	Per cent.	No.	Per cent.
Prior to onset of diabetes	11		17*	15		
Pre-insulin era**	57	95	21	21	11	19
Insulin era†	69	96				
Our cases‡	44	77				14

\*See table "Stillbirths" Table

\*\*Dead undelivered, miscarriage, and small miscarriage, therapeutic abortions.

†Unknown therapeutic abortions, 13

‡Therapeutic abortions.

*Physiology of pregnancy* Many physiological processes of pregnancy are capable of aggravating a pre-existing fault of sugar metabolism. Pregnancy, which is a great strain upon the metabolism of carbohydrates for the non-diabetic women, of necessity is a far greater carbohydrate strain for the diabetic. Notable in this respect is the rise of the basal metabolic rate due either to the growth of the products of conception (38), although this does not explain the rise which continues after delivery, or to the hyperactivity of the thyroid pituitary and adrenal glands. Microscopic changes, indicative of increased activity of the thyroid gland during pregnancy, and biological assay measuring an increase of the secretion of this gland have been demonstrated. When carbohydrate metabolism is at stake protein and fat metabolism will also fail. Even in the non-diabetic, the alkali reserve drops and ketone bodies (38) appear in the blood and urine. With such a background, it is remarkable that the successful termination of pregnancy has occurred in as many as two-thirds of all our diabetic cases.

Many questions of practical, theoretical, and ethical importance arise in this study and at present the answers are often speculative rather than determined. First, what is the relative fertility of the diabetic? Second, when does the glycosuria of pregnancy indicate true diabetes? Third, is pregnancy a precipitating cause of the disease? Fourth, what is the effect of diabetes upon the outcome of pregnancy? Fifth, what is the effect of pregnancy upon the course of diabetes and upon the future health of the diabetic woman? Sixth, what is the best method of diabetic and obstetric management? Seventh, what is the effect of the disease diabetes upon the future health of the child? Eighth, what are the child's chances of inheriting diabetes?

*Fertility in diabetes* The lack of fertility of the diabetic woman, which was long recognized in the pre-insulin era, has in great measure been corrected in proportion to the extent of the control of the disease. In uncontrolled diabetes, delayed maturity and long periods of amenorrhea still occur, but unlike what occurs in other diseases, the normal menstrual cycle of the diabetic can be re-

established even after a cessation for a period of years. The total pregnancy rate in our series is 10 per cent and the yearly rate 1.5 per cent.

Although in our own series the pregnancy rates in the insulin and pre-insulin eras are essentially the same, the clinical picture is different because the severe diabetic did not become pregnant prior to insulin therapy. The pregnancy rate in the pre-insulin era in the series of other authors has varied from 2 per cent in the London Hospital (35), and 5 per cent in Von Noorden's cases (20), to 6 per cent in Lecorche's (17) series of patients. The increase in the insulin era was greater in the London Hospital series than in ours, the former having risen to 15 per cent and the latter to 10 per cent, whereas the Mayo Clinic (23) in 1926 reported only 4 per cent.

The underlying cause of lack of fertility in uncontrolled diabetes is not definitely known. The basis may be hormonal, dietary, or nutritional. Either excess or lack of pituitary prolactin is a possible cause. Depression of the activity of the other endocrine glands probably occurs when diabetes is uncontrolled and the patient undernourished. The appearance of the diabetic dwarf is thus presumptive evidence of a functional hypoactivity of the pituitary gland. Hypoactivity of the gonadotropic factor of the pituitary would result in lack of estrin. Parisot has described the disappearance of graafian follicles in diabetes. Atrophy of the uterus has been described by von Grafe, and we have observed lack of development of the genital tract at autopsy in 4 young patients whose diabetes was of long standing. Under insulin therapy and adequately controlled diabetes, not only has long standing amenorrhea disappeared, but pregnancies have occurred in such cases, and, even more remarkable, in 2 of our pseudo dwarfs (Case 8256 and Case 6319).

*Diagnosis of glycosuria* The recognition of diabetes during pregnancy may be difficult indeed, for starvation, hyperactivity of the thyroid, pituitary and adrenal, and depletion of glycogen occur, and each one is capable of lowering tolerance for sugar. Glycosuria, apparently benign in nature, occurs so commonly in pregnancy that some writers go so far as to

say that if enough specimens of the urine of the pregnant patient are examined, one or more will be found to contain sugar in amounts varying from traces to several per cent, and yet the blood sugar remains normal. The reported incidence of glycosuria in non-diabetic pregnancies varies from 35 per cent (25) to 66 per cent (7) and in these statistics the sugar was identified as glucose.

Hyperglycemic curves after sugar tolerance tests have been reported by Pillman-Williams and Richardson, who classify them as benign. Skipper has demonstrated a plateau curve. In our own series of patients, the diagnosis of diabetes is made as in all other patients on the rise or peak of the curve. Whether the curves are normal or abnormal the patient should be observed for a period of years.

*Pregnancy as a cause of diabetes.* Since only 5 per cent of our female patients of child bearing age have had onset of diabetes during pregnancy pregnancy does not appear to be an inciting or at least a common inciting cause of diabetes. Potential diabetics (27-40) (the children of two diabetics, the homologous twin of a diabetic) have not developed the disease at this time and under 45 years of age, more males than females contract diabetes (Table III). The reverse would be expected if pregnancy precipitated diabetes.

TABLE III.—SEX AND THE ONSET OF DIABETES

Decade of onset of diabetes	Male per cent	Female per cent
3		6
	24	
		24

Diabetes incidence increases, however at other times when the pituitary prolactin of the blood is high and at such times an existing diabetes is often made more severe for not only is the peak of incidence in females at 12 (39) and 50 (4) but diabetes is increasingly difficult to control during catamens and at the time of menopause.

*Effect of diabetes upon the course of pregnancy.* The background of diabetes favors the development of the accidents of pregnancy in

proportion to lack of control of the disease. Abortions and early miscarriages occur with relatively greater frequency in diabetic women after onset of the disease. Twenty-two per cent of our patients aborted in the pre-insulin era, compared with 17 per cent in the insulin era, and 11 per cent in these same women prior to the onset of diabetes.

Premature expulsion of the fertilized ovum may be due to diabetic or non-diabetic causes. Among the diabetic causes we must consider a lethal factor in the egg, hypoglycemia, acidosis deficiency diet or lack of glycogen. The non-diabetic factor which however might secondarily be due to diabetes is excess of pituitary prolactin with consequent depression of the function of progesterin. If the fault lay in the primary cell because of diabetes, one would expect the wives of diabetic men to abort as frequently as do diabetic women and this is not the case. Lack of glycogen is possible. The studies of Simon show that the fertilized ovum implants itself in that portion of the uterus which has the richest supply of glycogen. In uncontrolled diabetes, glycogen deposition is abnormal. Faulty nidation may result from depression of progesterin.

Hypoglycemia (30) though capable of starting uterine contractions, probably is not an important factor because abortions occurred even more frequently in the pre-insulin era. It appeared to be the cause of abortion in one patient Case 7249. Two other patients, Case 8356 and Case 3040, had hypoglycemia with loss of consciousness and convulsions, and were delivered of living babies at term.

Acidosis appears to be somewhat more harmful. However only 5 of the 15 patients who miscarried had acidosis including one with chemical coma. Twelve had poorly controlled diabetes. The true accidents of diabetes thus appeared to play a minor rôle in the termination of early pregnancies. Factors secondary to uncontrolled diabetes, such as faulty storage of glycogen and disturbed endocrine function need further investigation and in fact, this study has already been started.

*Stillbirths.* The investigation of the cause and the means to prevent the occurrence of stillbirths in diabetics is the most important problem in pregnancy complicating diabetes.

The incidence of stillbirths has not been reduced adequately in the insulin era since 17 per cent of the pregnancies resulted in stillbirths when even 6 per cent is considered a high stillbirth rate. In patients under our care, it has been reduced to one-third of the rate of the pre-insulin era and insulin era as a whole but it still occurs twice as frequently in diabetics as it does in non-diabetics (see Tables I and II).

Mechanical, chemical, hormonal, or structural abnormalities may cause stillbirths in diabetes. Maternal complications such as syphilis, heart disease and anemias were not found in this series. Of the mechanical factors, the size of the baby is the most important. Sixty per cent, or 33 of our babies for whom we had data, weighed over 8 pounds, compared with 9 per cent of 100 babies reported by Carreno for a series which included one diabetic. The average weight for babies in the insulin era slightly exceeded the weight of babies in the pre-insulin era. The size of babies (2) of diabetic mothers is so striking that some clinicians call attention to the fact that a large baby may indicate maternal diabetes, and such mothers should be investigated for the disease. Nevinsky and Schretter have reported a baby classified as a giant, and observed changes in the fetal hypophysis. Obesity of the fetus in the diabetic may be due to overnutrition from hyperglycemia, lipemia, or to edema which is a direct result of exogenous insulin. Possibly it is inherited obesity. Perhaps it is due to hyperactivity of the fetal or maternal pituitary gland. Permeability of the placenta to fat and pituitary-like substance is known. Exogenous insulin is not the likely cause because the babies in the pre-insulin era were large. The greatest growth of the embryo occurs in the last 2 months, at which time the blood sugar is generally normal. Extreme hyperlipemia has not been observed in our own pregnancy cases. Thus insulin, fat, and sugar do not seem to be the probable causes of the overgrown fetus. The mechanical difficulty of labor resulting from the delivery of the large baby, cannot be the most common cause of fetal death, though undoubtedly it increases the stillbirth rate. Two-thirds of

these fetuses were macerated, or an incidence of 1 in 7 in the insulin era compared with an incidence of 1 in 83 for non-diabetics, reported by Dippel from the obstetrical service of the Johns Hopkins Hospital. This leads us to search for a cause which might interfere with the nutrition of the child or a direct lethal agent, active the last 4 weeks of pregnancy. Small placentas which might result in subnormal nutrition have not been found in our cases.

Hydramnios, which also endangers the life of the fetus, is believed to occur in diabetes, and is held as a cause of fetal mortality. We have observed it but twice. This is surprising because the common causes of hydramnios, namely fetal deformities, large children, and maternal toxemias occur in diabetes. The origin may be chemical. Grafe has demonstrated an excess of glucose in the amniotic fluid in 5 of 10 diabetic pregnancies. Better control of glycemia may have resulted in correction of this complication.

The abnormal chemistry of the maternal blood may have its effects upon the fetus. Reports exist to the effect that maternal and fetal blood sugar and alkali reserve are the same and that the low alkali reserve is the factor which kills the fetus in toxemias of pregnancy. The blood of the newborn baby and maternal bloods in 3 of our cases show the following:

In this small series the level of the blood sugar, plasma carbon dioxide combining power, non-protein nitrogen, cholesterol and chloride of the baby and mother were not identical. Thus we have no proof that imbalance of carbohydrate, fat, mineral metabolism, or acidosis of the mother directly influences the child (Table IV).

In the insulin era Cases 12751, 7565, 3677, 2776 developed coma during pregnancy. In the 3 former, coma was not followed by death of the fetus. Stillbirth was the outcome of Case 2776, but the fetus was macerated and death of the fetus antedated the onset of coma.

Although the passage of insulin through the placenta has been demonstrated, the production of hypoglycemia in the fetus does not seem probable. Britton injected large amounts of insulin, producing maternal hypoglycemia



TABLE IV—A COMPARISON OF CHEMICAL DATA IN MOTHER AND INFANT

Case 7357 Sept. 4, 1914	Blood sugar per cent	Vol. per cent Fleming L.D. Coulter avg 20 per cent	Mean pre- insulin sugar per hundred cc.	Obstetrical sugar per 100 cc.	Obstetrical sugar per 100 cc.
Infant (Cord)	1.4	19			
Mother	40	26	29		
Placenta	26	26	26		
Case 7422 Sept. 16, 1914					
Infant (Cord)	16	22	22	26.4	
Mother	22	22	27	26.6	
Placenta	26	26	26	26.7	
Case 7411 Sept. 14, 1914					
Infant (Cord)	17	26	1.4		30
Mother	29	26	2.3		26.6

with little or no apparent effect upon the fetus. Certainly none of our own patients had severe hypoglycemia as an attributable cause of stillbirth. Furthermore, Flah and Woods have shown that in a pregnant woman near term starvation for 50 hours in the last month of pregnancy is frequently followed by hypoglycemia and onset of labor without injury to the fetus. The report of Gray and Feemster and others suggesting that endogenous hypoglycemia is a cause of fetal death is an interesting possibility. Better control of diabetes has certainly reduced the stillbirth rate. Pathological evidence in favor of this theory is striking but the normal fetal pancreas has large islands, and the new born and premature infant relatively low blood sugar levels.

Disease of the uterus, age of the mother, parity or duration of diabetes, may be factors producing any of the failures. Age of the mother had its effect, since the younger and older mothers lost more children than did the intermediate group.

Multiparity had no favorable effect. The outcome of multiparous pregnancies showed only 50 per cent successes. The outcome of primiparous pregnancies without cesarean section was 69 per cent, and with cesarean section was 75 per cent.

Factors which favor ready control of diabetes, favor the number of live births. Thus is

TABLE V—AGE OF DIABETIC MOTHERS IN RELATION TO SUCCESSFUL OUTCOME OF PREGNANCY

Age in years	Successful outcome of pregnancy per cent
Under 20	25
20-24	33
25-29	66
30	30

apparent in both the pre-insulin and insulin eras. In the first year of diabetes, the disease is most readily controlled, and here we find the greatest number of live births. In the insulin era the same is true. The percentage of live births is 85 in the first year of the disease, and drops to 50 per cent in all other years of diabetes.

The demonstration of excessive prolan in the blood and urine of patients with toxemia by Smith and Smith, and the excess of toxemias and eclampsias in diabetes in our own series of cases, give us a new lead in the search for the lethal factor active the last 4 weeks of diabetic pregnancies. In accordance with this theory of possible damage to the fetus from excess of prolan is the result of the experiment of Snyder who found that the administration of prolan (antuitrin S) to pregnant rabbits resulted in prolongation of gestation and of death and maceration of giant postmature rabbit fetuses.

Maternal mortality in contrast to the high fetal mortality has been low. In the combined eras it was 5 per cent, in the pre insulin era 5 per cent, and in the insulin era 5 per cent. The deaths in the pre-insulin era were all diabetic; the deaths in the insulin era were all obstetric.

*Maternal accidents.* The background of diabetes appears favorable to the development of toxemia and eclampsia, the incidence of eclampsia being 5 per cent compared with an average of 0.3 per cent in a non-diabetic series. The younger the patient the greater the chance for development of eclampsia because the incidence in former juvenile diabetes was 13 per cent. It is possible that diabetics are predisposed to develop an endocrine imbalance similar to that described by Smith as typical of toxemia and eclampsia.

Pernicious vomiting has occurred but once. Premature separation of placenta and extra-uterine pregnancies have not occurred. There was but 1 breast abscess, and 3 cases of puerperal sepsis.

*The effect of pregnancy upon diabetes (a) Tolerance* This brings us to the next problem, the course and treatment of diabetes during pregnancy. The question whether or not pregnancy alters the course of diabetes is still debated. In the literature (8) one finds reports of gains in tolerance for carbohydrate and an equal number of reports of losses of tolerance for carbohydrate. The fairly general consensus of opinion is that a loss occurs in the first trimester, a status which is stationary in the second, and either a gain or loss of tolerance in the third. In the pregnant diabetic dog, Carlson and Drennan were able to demonstrate a great gain in tolerance during pregnancy. That insulin circulates through the placenta or the mother is shown in the experiment of Pack and Barber. Insulin injected into the fetus of a goat was followed by the production of hypoglycemia in the mother. Some few patients in our series, notably one after coma, Case 7565, omitted insulin entirely in the last trimester. A crude analysis of our cases shows that half of the number with suitable records had milder diabetes during pregnancy than at any time before or after, but others have had more severe diabetes. Furthermore, we observed one patient, Case 6506 for some weeks after the death of the fetus, and her insulin requirement did not alter.

During the course of pregnancy in the severe juvenile type of diabetes, there has practically never been a gain of tolerance for carbohydrate. The weight of the newborn baby's pancreas is only 1.5 grams, the weight of the adult pancreas is 100 grams. If we assume that 100 units of insulin are produced by the 100 gram pancreas of an adult, 1 unit is produced per gram. The child's pancreas, on this basis, would hardly secrete more than a single unit. Fetal pancreas, however, probably contains 10 to 15 times as much insulin as adult pancreas. In all cases this constant source of insulin would be of value. It would be an adjunct to treatment in twin pregnancies, as in the case re-

ported by Lawrence (15, 16). Our own patient with twin pregnancy showed no great gain in tolerance. The multiple pregnancies of animals may account for the gain reported by Carlson and Drennan. Under-nutrition may explain whatever gain in tolerance occurs (1, 18). We thus conclude that a gain or loss of tolerance is an individual factor.

*Effect of pregnancy upon the direct complications of diabetes (b) Acidosis* The direct complications of diabetes, coma and hypoglycemia, are to be feared during pregnancy, labor, and the puerperium. Acidosis and coma are to be feared during pregnancy because a low alkali reserve, glycogen depletion, and increased metabolic rate occur.

The plasma combining power for carbon dioxide was found to be low in 12 of 13 patients carefully studied, and 6 had clinical signs of coma. These patients demonstrated that the blood sugar was not proportionately high. If coma occurs during the course of labor, treatment is difficult, for labor deepens coma. As soon as delivery is completed chemical recovery follows.

*(c) Hypoglycemia* Hypoglycemia in pregnancy is usually the result of poor treatment. It occurs when the dosage of insulin is increased in the presence of a low renal threshold. During labor it results from increased utilization of carbohydrate, and during the puerperium from lactation.

*Management of diabetes and choice of delivery* The dietary management of diabetes in pregnancy consists in supplying the mother with enough calories to correspond with the rise of metabolism, which at term has probably increased 20 per cent, in providing for the baby's need for glycogen, and a division of meals which will insure the greatest protection against acidosis, glycogen depletion, and hypoglycemia. The special problems for each trimester must be considered separately.

The early nausea and vomiting of pregnancy can best be treated by hourly feeding and administration of insulin at three hour intervals. This of course may need to be supplemented by intravenous glucose. A safe diet would be carbohydrate 150, protein 60, fat 60 to 80 grams, and insulin every 3 hours—15 units if the Benedict test is red, 10 units if the

test is yellow or orange and 5 units if yellow green.

The second trimester demands but little special care. The caloric and carbohydrate content of the diet should be increased. The problems of the third trimester are more baffling. By this time the baby needs 50 grams of glucose daily. The renal threshold is low and insulin must be increased cautiously. The basal metabolism is at its highest and the alkali reserve at its lowest level. Our diet averages carbohydrate 175 to 200 grams, protein 60 to 80 grams, and fat as needed. The urine should contain small quantities of sugar. Frequent blood sugar determinations will help to prevent hypoglycemia.

During normal delivery the patient must receive 200 to 300 grams of carbohydrate. If a surgical delivery is chosen the procedure is the same as at any operation—carbohydrate 100 grams by mouth or intravenously during the first 24 hours after delivery and insulin every 3 hours according to the degree of reduction of the qualitative test for glucose.

*Choice of delivery.* The choice of delivery for the diabetic is debated. One must seriously consider the patient's background, the handicap of a chronic disease, a future in which the hazards of mortality and morbidity are greater than the average. There is also an economic hazard—periods of time when because of illness the diabetic is unable to perform her work, and her duties must be assumed by some one else—the extra cost of medical care, diet, insulin and periodic health examinations. To the element of the mother's fear arising from normal pregnancy is the added element of fear of accidents to her child and to herself because of diabetes. Her physical condition for the mechanical strain of labor is in inverse ratio to the duration of her disease and in direct ratio to the control of her disease. Dr. Joslin has often said that to obtain the true age of our patients, we must add the duration of the disease to the chronological age. Thus a youthful diabetic at 25 years of age, the onset of whose disease was at 10 years—and this will be the problem of the future—is actually 40 years of age. Her disease has predisposed her to arteriosclerotic disease of the heart, eyes, and kidneys, to increased susceptibility to

tuberculosis, possibly to depression of the hormonopoietic system, to anemias and damage of the liver has made her muscles atrophic and poorly nourished has predisposed her to degeneration of the peripheral nerves, and increased her susceptibility to infections with the colon bacillus and pyogenic cocci.

Prolonged difficult labor normal or induced has disadvantages for the diabetic. Those of immediate importance are the early exhaustion of the glycogen reserve and the danger of sepsis, the danger of hyperinsulinism exogenous and endogenous, and the danger of acidosis. The secondary considerations are the added handicap of a torn perineum or cervix and consequent indication for later surgery. These patients are not physically fit for numerous pregnancies. The baby has not the vitality of the child of the non-diabetic, and great is the risk of injury from long labor to this large overdeveloped but at the same time, flabby child. Furthermore, the induction of labor does not answer the problem as well as cesarean section because induction of labor is not safe until the cervix is soft, and the cervix may not be soft until after the baby has died.

Prolonged narcosis in the presence of low alkali reserve and glycogen depletion is a perfect setting for the onset of true diabetic coma. Everywhere it is evident that the modern woman demands safe labor, freedom from unnecessary pain, a reasonable length of labor and a complete restitution. In our opinion the diabetic deserves not less.

*Outcome of pregnancies in patients with onset of diabetes in childhood.* The very young diabetic, the onset of whose disease occurred in childhood demonstrates to us even more than the older patients, that the pregnant diabetic requires accurate control of diabetes throughout pregnancy, an intimate association between internist and obstetrician and double the supervision of the average pregnancy cases.

The maternal mortality in this group of 22 pregnancies in 15 mothers was high (Table VI). Two who were not under our care at the time died: 1 of eclampsia and 1 following a therapeutic abortion, making the maternal mortality for this special group 13 per cent in the insulin era. Of the pregnancies which came to

TABLE VI—PREGNANCIES IN DIABETES WITH ONSET OF DIABETES IN CHILDHOOD

	Insulin	Duration of diabetes years	Onset age years	Date onset	Date pregnancy	Delivery	Outcome	Complications
1753	+		5	1916		Normal	Living birth	o
214	+	12	12	1920	1932	Normal	Living birth	o
254	+	13	9	1919	1942		Miscarriage	o
27,6	+	11	8	1921	1932	High forceps	Stillbirth	Coma—pyelitis arteriosclerosis
	+	12	8	1921	1933		Therapeutic abortion	
502	+	12	14	1922	1934		Therapeutic abortion	Coma death
3040	+	9	1	1922	1931	Normal	Living birth	Arteriosclerosis
416	+	11	14	1922	1933	Forceps	Living birth	Puerperal sepsis
45-6	+	5	14	1923	1928	Normal	Stillbirth	Arteriosclerosis
	+	7	14	1923	1930	Normal	Stillbirth	Arteriosclerosis
	+	7	14	1923	1930		Miscarriage	Arteriosclerosis
	+	8	14	1923	1931	Induced	Living birth	Arteriosclerosis
	+	10	14	1923	1933	Normal	Stillbirth	Arteriosclerosis
	+	12	14	1923	1934	Cesarean	Living birth	
	+	11	14	1922	1932	Induced	Stillbirth	Death—eclampsia
7014	+	14	14	1919	1933	Cesarean	Living birth	o
7251	—	10	13	1924	1934	Cesarean	Living birth	o
7407	+	5	14	1923	1932		Therapeutic abortion	
	+	6	14	1923	1934	Cesarean	Living birth	Sepsis
856	+	6	14	1923	1931	Cesarean	Living birth	Toxemia
9093	+	3	14	1931	1934	Normal	Living birth	o
11563	+	2	15	1932	1934	Cesarean	Living birth	Eclampsia

term, 12 resulted in living births, and 5 in stillbirths. The incidence of stillbirth is thus five times that of the Johns Hopkins Hospital series of non-diabetics used as control. Miscarriages were not frequent, these occurred only twice (10 per cent). The incidence of eclampsia was 13 per cent and of non-fatal puerperal sepsis, among patients coming to term was 12 per cent. Two patients developed coma and 2 hypoglycemia. None developed a true gain in tolerance for carbohydrate. Two of the babies developed unexplained edema.

At the ages of 19, 22, and 23, 3 of the mothers had evidence of arteriosclerosis, 2 with demonstrable retinal hemorrhage, and 1 with peripheral sclerosis, demonstrable by X-ray.

**Lactation.** Lactation is poor perhaps because of relative undernutrition or lack of the specific lactogenic hormone. An analysis of milk of one diabetic patient showed nothing abnormal. None of our patients has been able to produce more than a few ounces of milk

daily, when the diet has contained 2500 calories. Sherrill reviewed the literature on this subject and reported his own cases of Diabetic animals, as well as diabetic patients fail to lactate normally.

**Effect of diabetes upon the child.** Congenital defects occur frequently in children of diabetic mothers. This is evident both in the series reported in the literature (8), and in our own patients. In our pre-insulin and insulin series of 166 babies, there were 7 abnormal. One was microcephalic, 1 a Mongolian idiot, 2 had congenital heart disease, 1 atresia of the gastro-intestinal tract, 1 achondroplasia, and 1 was a monster. The incidence of defects among stillbirths was 1 in 7 compared with 1 in 61 for consecutive cases at the Johns Hopkins Hospital, reported by Dippel. This included 1 diabetic. Two of the babies developed unexplained edema, 7 died in the first week, and 1 other died in the first year. Thus a 5 per cent mortality occurred in the first

year which was exactly the mortality of the non-diabetic series reported by Peckham. Our neonatal mortality exceeded the control series slightly. The former amounted to 4 per cent and the latter 3 per cent. Thus it would appear that if a child of a diabetic mother is born alive, the life expectancy is good.

**Inheritance.** The problem of inheritance of the diabetic (39, 40, 10, 26, 27, 28) is indirect here rather than direct, for according to our present belief the potentiality for developing diabetes is inherited as a Mendelian recessive trait and the child cannot inherit the disease from one diabetic parent alone, but only from two diabetics, a diabetic and a hereditary carrier or two hereditary carriers. The children of these diabetics, however, will all be hereditary carriers of the disease. Based upon an incidence of 0.3 per cent diabetics in the general population we estimate that already 25 per cent of our entire population must be carriers of the disease and such pregnancies increase the carrier incidence.

#### CONCLUSIONS

Premature delivery of the fully developed though chronologically premature infant of the diabetic mother by cesarean section is the obstetrician's successful answer to the challenge. The cause and cure of the overspensing of the fetus remain in the speculative stage, but the study of the hormones in diabetes offers hope for the correct solution.

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#### BIBLIOGRAPHY

- ALLY, F. M. *Am J Physiol* 930, 54, 45
- BALBO, Arch. de Endocrin y Metab., 930, 4, 3
- BLOCH, W. O. and SCHENKEL, W. *Arch f Gynaek.*, 93, 143, 5
- BRITTON, S. W. *Am J Physiol* 930, 93, 78
- CARLSON, A. S. and DREYMAN, F. M. *Am J Physiol* 9, 5, 36
- CARRERO, CARLOS. *Arch argent de Pediat* 1933, 4, 75
- CHART, L. A. *Canadian M. Ass J* 1933, 26, 279
- COLEMAN, W. S. and SEACK, I. L. *New York State J Med* 933, 3, 780
- DEPPEL, A. S. *Bull Johns Hopkins Hosp* 934, 20, 44
- GOONKA, L. and WILLIAMS, O. B. *Am J Physiol* 92, 86, 3, 3
- GRANT, VON. Cited by Skupper
- GRAY and FENCSTER. *Arch Path & Lab Med* 930, 348
- HOLMAN, A. and M. THOMA, A. *Am J Obst & Gynec.* 934, 87, 95
- JOSLIN, E. P. *The Treatment of Diabetes* 4th ed Philadelphia Lea & Febiger 928
- L. WILKIN, R. D. *Proc. Roy Soc Med* 937, 9
- Idem. *Quart J Med* 930, 22, 197
- LECOMTE. *Ann de gynec d'obst* 88, 24, 5
- MARLOWITZ, J. and SCHWARTZ, S. *Am J Physiol* 937, 79, 133
- NEVILL, H. and SCHWARTZ, G. *Zentralbl f Gynaek.* 93, 54, 740
- NOBLEMAN, VON. *Am J Obst & Gynec.* 934, 7, 7
- PAGE, O. F. and BARNER, D. *Am J Physiol* 1930, 90, 466
- PARSONS. Cited by Skupper
- PARSON, E. RANALL, L. WILSON, R. M. *Med Cha N America*, 936, 679
- PERHAM, C. H. *Bull Johns Hopkins Hosp* 1934, 34, 36
- PILLMAN WILLIAMS, E. C. and WILSON. *Quart J Med* 930, 22, 493
- PINCUS, G. and WHITE, P. *Am J Med Sc* 1933, 86
- Idem. *Am J Med Sc* 934, 88, 29
- Idem. 78
- PINCUS, G. JOSLIN, E. P. and WHITE, P. *Am J Med Sc* 934, 83, 6
- PLAHL, E. D. and WOODS, F. D. *Am J Obst & Gynec.* 934, 7, 295
- RICHARDSON, R. and BITTER, R. S. *Am J Obst & Gynec.* 933, 24, 65
- SEEDHILL, J. W. *Calif & Western Med* 934, 61, 40
- SHROY, H. *Am J Obst & Gynec.* 934, 7, 284
- SHRYVER, A. G. *Am J Physiol* 1933, 7, 72
- SKUPPER, E. *Quart J Med* 933, 253
- SMITH, G. V. S. and SMITH, O. W. *Am J Physiol* 934, 107, 38
- STEWART, F. *Bull Johns Hopkins Hosp* 1934, 34
- STEWART, H. J. and COOPER, J. F. *Bull Johns Hopkins Hosp* 930, 47, 38
- WHITE, FRANCES. *Diabetes in Childhood and Adolescence* Philadelphia Lea & Febiger 93
- WHITE, FRANCES, JOSLIN, ELLIOTT P. and PINCUS, G. *J Am M Ass* 934, 1, 105

## COMPOUND COLORED ALCOHOLIC SOLUTION OF MERCURIC CHLORIDE FOR SKIN DISINFECTION

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WE have been studying various solutions used in surgical practice for disinfecting the skin. The *in vitro* disinfecting powers of most of these solutions are satisfactory. Tinker and Sutton have reviewed the *in vivo* disinfecting power of several commonly used skin antiseptics. Some were found to irritate the skin. All of these solutions are too expensive. We have made up more than a hundred different solutions and studied various properties of each. Our object was to make up a solution that would possess the following properties: (1) a high phenol coefficient, (2) the power to penetrate the skin, (3) the power to remove fat from the skin, (4) a color so as to define the operative field, (5) the ability to lose the color promptly after operation, (6) it should not irritate, blister or burn the skin, (7) it must be inexpensive.

The bacteriological technique used to determine disinfecting power and phenol coefficients was carried out according to the recommendations set forth by the U. S. Department of Agriculture. (1) The tinctures and aqueous solutions of various disinfectants used in the tables in this paper for comparison with our new solution are the same as contained in the *New and Ven official Remedies*.

The formula we have developed in our laboratory is given in Table I.

TABLE I—FORMULA FOR ONE LITER OF THE COMPOUND COLORED ALCOHOLIC SOLUTION OF MERCURIC CHLORIDE

	Amount	Per cent
Ethyl alcohol (95%)	525 c cm	50
Acetone U. S. P.	100 c cm	10
Mercuric chloride	1 gm	1/1000
Hydrochloric acid	7.5 c cm	0.75
Chrysoidin Y	2 gm	1/500
Distilled water	367.5 c cm	
Total amount of solution	1000 c cm	

**Alcohol.** Alcohol lowers surface tension and is of itself a disinfectant. The penetration of dissolved mercuric chloride is facilitated and

some defatting effect is obtained by using alcohol. We have varied the alcohol content from 10 to 50 per cent. It was found that 50 per cent alcohol was satisfactory. Lower alcohol content showed a rapid decrease in the disinfecting power. Higher alcohol content than 50 per cent showed some increase in disinfecting power but not enough to warrant the additional expense.

**Acetone.** Vaseline was rubbed into the skin. All excess was wiped off with dry gauze. Varying concentrations of acetone in 50 per cent alcohol were used to defat the skin by surface rubbing. This is usually carried out in preparing the skin for surgical operative procedures. A drop of water was put on the prepared skin area to test the defatting effect. If the water spread uniformly into a thin layer, we considered the skin free of vaseline. Ten per cent acetone was the smallest amount we could use to satisfactorily defat the skin.

**Hydrochloric acid.** The HCl ion is a good disinfectant. We have found that if sufficient hydrochloric acid was added to obtain the acid disinfecting action, there was a burning sensation after application. Four per cent hydrochloric acid has been used in many of our solutions. This enhances the disinfecting power, but the solution was objectionable as already mentioned. We have used the amount of hydrochloric acid which was found to increase the disinfecting power of the mercuric chloride by increasing the ionization and hence making more mercury-ions available. We chose 0.75 per cent hydrochloric acid as the amount best suited for a non-irritating skin disinfectant. Table II gives a typical protocol of such an experiment.

**Dye or coloring material.** We were desirous of obtaining a dye which would color the skin in such a way as to clearly define the field treated with the skin disinfectant. The dye should not be of such a color as to subconsciously indicate hyperemia, passive congest-

TABLE II

Mercuric chloride 1:1000, alcohol 50 per cent and acetone 1 per cent was used as our stock solution. Varying amounts of hydrochloric acid were added to this stock solution.

Hydrochloric acid (per cent)	Highest dilution killing in 10 minutes
	30,000
	30,000
3	1:30,000
3	30,000
0.5	1:1,000
7	15,000
8	15,000
	5,000
4	10,000
6	50,000

TABLE III

The highest dilution necessary to kill *Staphylococcus aureus* (No. 400 strain) in 10 minutes but not in 5 minutes at 30 degrees C.

Alcohol acetone solution of (concentrated in A.C.)	Highest dilution	Percent coefficient
Chrysoidin Y 0.5%	50	3.6
Mercuric chloride, 0.5%	40	1
Phenol	70	

tion or any other abnormal circulatory or system reaction. The dye should disappear from the skin within a day after its use. We used 85 different dyes in our work. Chrysoidin Y has proved most satisfactory in our hands. The color of the skin resembles that of tincture of iodine. The color gradually fades and disappears within 24 hours after application.

Chrysoidin Y is not readily soluble in water but is soluble in alcohol, hence it was thought best to test its germicidal power in an alcohol acetone solution. We prepared these solutions according to the method outlined by Scott and Hill. Two per cent solutions were made up in 50 per cent alcohol, 10 per cent acetone and 40 per cent water. Table III gives the results of our tests with chrysoidin Y and mercuric chloride in dilutions necessary to kill *Staphylococcus aureus* in 10 minutes but not in 5 minutes at 30 degrees C. Chrysoidin Y was found to give a slight precipitate in the solution after standing several days. We were informed by the National Aniline and Chemical Company that the usual product contained 25 per cent impurities. They purified a sample containing 9 per cent chrysoidin Y and 4 per cent moisture. No precipitate is formed when this purified dye is used.

We were surprised to find the tinctorial ma-

TABLE IV

Highest dilution of disinfectant killing *Staphylococcus aureus* in 10 minutes but not in 5 minutes at 30 degrees C.

Disinfectant	Highest dilution	Percent coefficient
Compound alcoholic solution		
mercuric chloride colored	5,000	337
Tincture of iodine	9000	25
Tincture of mercuric iodine	4000	17
Tincture of mercuric iodine	6000	45
Tincture of mercuric iodine	1:30	1
Phenol	70	

TABLE V

Highest dilution of aqueous solutions of disinfectants killing *Staphylococcus aureus* in 10 minutes but not in 5 minutes at 30 degrees C.

Disinfectant	Highest dilution	Percent coefficient
Mercuric chloride 0.00	5,000	186
Mercuric chloride 1.00	2,000	57
Hydrochloric acid 1%		
Mercuric iodine	0,000	145
Mercuric iodine	4,000	57
Mercuric iodine 3%	25	5
Phenol	70	6

terial we had chosen possessed of itself a definite disinfecting power.

The relative disinfecting power of this compound colored alcoholic solution of mercuric chloride in comparison with other alcoholic solutions of disinfectants. Table IV summarizes the results we have obtained.

Aqueous solutions of various disinfectants were also compared. We used aqueous solutions of mercuric chloride and mercuric iodine with 1 per cent hydrochloric acid in water. Table V summarizes the results of these studies.

The formula we have used has been developed under controlled laboratory conditions. The solution was kept in tightly stoppered containers. We realize the skin disinfectant used in routine surgical practice would not be handled in this manner. We have, therefore, modified the constituents of this solution to facilitate ease of preparation and to allow for evaporation when placed in open vessels and re-used. The formula we suggest for practical purposes is as follows:

Fibryl alcohol (95%)	600 c. cm.
Aniline (U. S. P.)	200 c. cm.
Mercuric chloride	grs.
Hydrochloric acid (concentrated)	10 c. cm.
Chrysoidin Y	grs.

Make up to 1000 c. cm. with water.

We prepare this new compound colored alcoholic solution of mercuric chloride for one dollar and sixty cents per gallon in our laboratory. If large quantities of ingredients are purchased the price would be lower. Tincture of iodine (U. S. P.) costs approximately four dollars and two cents and a per cent tincture of iodine costs us two dollars and sixty-five cents per gallon. The prices quoted us from various sources for tinctures of metaphen, merthiolate, and mercurochrome were over twenty dollars per gallon.

This new compound colored alcoholic solution of mercuric chloride has been used as the disinfectant in 300 cases of gunshot automobile accidents, and other similar emergency

hospital cases. It has been used in 120 cases of neck surgery and 65 cases of abdominal surgery. The reports are favorable; no infections followed, and the non-irritating properties of this disinfectant were commented upon by the surgeons using the solution.

#### REFERENCES

1. KETCHUM and BAKER. United States food and drug administration methods of testing antiseptics and disinfectants. U. S. Department of Agriculture, Washington, D. C. Circular No. 198, 1931.
2. SCOTT and HILL. Action of mercurochrome and tincture of iodine in skin disinfection. *J. Am. M. Ass.*, 1929, 62: 111.
3. TINSLEY and SURTON. Inefficiency of most of the commonly used skin antiseptics. *J. Am. M. Ass.* 1926, 87: 1347.
4. *New and Non-official Remedies*. *Am. M. Ass.*, Chicago, 1923.



THE EARLY DIAGNOSIS OF CHORIOEPITHELIOMA<sup>1</sup>

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**B**EFORE the discovery of their pregnancy test by Aschheim and Zondek, the diagnosis of chorioepithelioma usually rested on the presence of profuse uterine bleeding, extensive metastases, and the finding of the tissue in the curettings. Now however since chorioepithelioma can be demonstrated by a positive pregnancy test, it appears that the diagnosis can be made early even before metastasis takes place and with a considerable degree of certainty by the judicious use of the Aschheim-Zondek or the Friedman test. Early diagnosis is the *leit motif* of this paper.

Maser and Edelken recently made a plea for the use of the Friedman test in cases of suspected chorioepithelioma because of the inadequacy of uterine curettage in the diagnosis, and these authors cite cases stressing the unreliability of curettage in the early diagnosis of the disease. Inspection of the pathological specimen in our first case proved to us conclusively that curettage could not have aided in the diagnosis; in fact, we would have been grossly misled by this procedure. We feel that diagnosticians should go one step further and follow every case of hydatid mole with pregnancy tests. Maser and Edelken came to the conclusion which we think well founded that abnormal uterine bleeding occurring within a few months after a mole pregnancy should not be treated by irradiation on the assumption that the bleeding is of the so-called functional type. We condemn the promiscuous use of radium in uterine bleeding at the cost of keen and finished diagnosis.

In the discussion of the paper by Maser and Edelken Longaker cited a case which had been under his care for about 18 months in which a positive diagnosis of chorioepithelioma had been made because of the persistently positive Friedman test. However his case remains unproven since, in the absence of clinical evidence he did not operate on this woman and she made a perfect recovery.

Since our first patient offered no clinical evidence at the time of the operation, we are in a philosophic mood as to whether or not these growths sometimes regress. This is a very interesting point and apparently no one can know whether such regression will take place or not. It is barely possible that she had such a tumor and that regression would have taken place eventually. In the discussion of the same paper Hoffman elaborated some very interesting ideas. We quote his statements verbatim.

The Aschheim-Zondek reaction is undoubtedly a most important adjunct in the diagnosis of chorioepithelioma. For purpose of prognosis, however its value is less certain. Clinically and histologically, it is almost impossible to differentiate between the benign and the malignant forms of this condition. Both may give a similar clinical picture and either may give rise to metastases. Indeed, some authorities believe that these two forms are identical and that the outcome of the case depends upon the amount of antitrophoblastic agents present in the host. Since the Aschheim-Zondek reaction is positive for both forms, it fails to aid in the task of differentiation, and we remain, as before, dependent upon the occurrence of death for the determination of what form it is with which we have been dealing.

Under the circumstances, therefore, it would seem best, before undertaking any radical procedure, to consider all factors, clinical and otherwise. The mere fact that a positive reaction has been obtained is not sufficient to justify such procedure. Emphasis should be rather placed upon the clinical evidence, especially when we recall that as yet it has not been established that a negative reaction rules out chorioepithelioma.

With due regard for the opinion of Hoffman, we cannot believe that it is justifiable to wait for metastasis in the face of persistently positive pregnancy tests before the operation is done, nor do we believe that we should temporize in the face of persistently positive pregnancy tests when we are sure that there is not a normal pregnancy in the uterus. Following this doctrine some operations might be done needlessly but the common good would be served. Whether or not a negative

<sup>1</sup>Read at the meeting of the Pacific Coast Society of Obstetrics and Gynecology, November 12, 1932, at San Diego, California, and at the meeting of the Pan American Medical Association, January 10, 1933, at San Francisco, California.

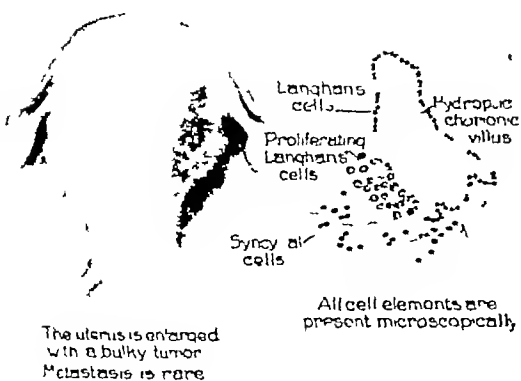


Fig 1

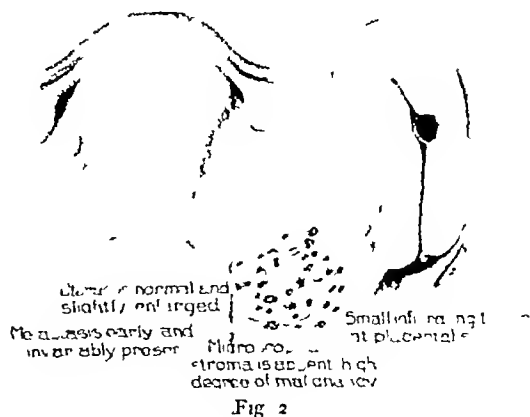


Fig 2

Figs 1, 2, and 3 Artist's drawings showing the physical and microscopic characteristics of Ewing's three types of chorioepithelioma. Fig 1 Choroadenoma (follows mole). Fig 2 Choriocarcinoma—follows labor, abortion and ectopic pregnancy, missed abortion and mole. Fig 3 Syncytial endometritis.

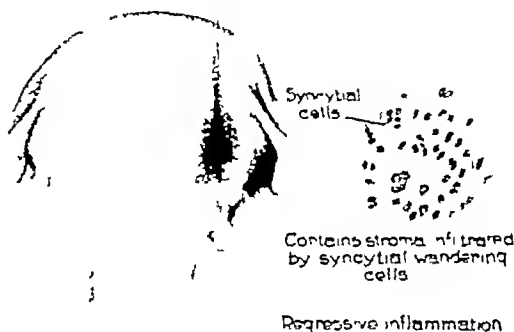


Fig 3

reaction rules out chorioepithelioma. Time and recorded study alone will determine. This fact and many others pertinent to the subject can be ascertained by following the dictum of Mazer and Edeiken that all cases of suspected chorioepithelioma should be checked by repeated Friedman tests and by following our further suggestion that all cases of hydatid mole be checked by the Friedman test.

There is a difference in response to ovary stimulating substances in rabbits of different ages. We noted in an early paper that follicle maturation and hemorrhage into follicles does occur in the rabbit ovary spontaneously in the absence of pregnancy intercourse or other known forms of artificial vaginal stimulation. We have never observed this ovarian activity in an animal younger than  $4\frac{1}{2}$  months of age. This activity must not, however, be confused with ovulation. It is certain that older animals are more susceptible to slighter degrees of stimulation than are the younger ones and it is our contention that the few false positive Friedman pregnancy reactions reported by other observers must be due to the presence of those unruptured hemorrhagic follicles that do occasionally occur in rabbits older than  $4\frac{1}{2}$  months. In our series of nearly 400 Aschheim-Zondek tests and over 800 Friedman tests we have less than 1 per cent false positive reactions.

We use animals at about 14 weeks of age, putting the upper and lower age limits at 12 to 18 weeks.

All of our specimens of urine are treated with toluol as soon as they are received. Decomposition and bacterial growth are prevented by this treatment. Saturation of the urine is accomplished with 2 drops of toluol to 1 ounce of urine. When a specimen arrives which is several days old and which appears decomposed it is easily detoxified by shaking with toluol and filtering through ordinary filter paper. It should not be injected until it is free from the putrefactive odor. More than one shaking with toluol and more than one filtering may be necessary, but this treatment does not seem to affect the accuracy of the test. Cloudy and foul smelling urine should always be treated in this manner. If this procedure is carried out routinely the mortality of animals will be reduced to a minimum. We

3. FRIEDMAN, R. S. Quantitative behavior of prolan A in testicular tests. *Am J Cancer* 933, 6 269
4. FREEMAN, P. Hydrated mole. *Am J Obst* 9 7 35 668
5. FUR, R. T. Chorionepithelioma proliferations in teratomata, especially in those of the testis, with three new cases. *J Am M Ass* 900, 46 548
6. GRENZNER, F. A. Ein Fall von metastatischem Chorionepitheliom durch die Archheim-Zondeische Reaktion diagnostiziert. *Zentralbl f Gynak* 93 33 543
7. HAHN, V. G. H. and BUDY, J. W. Massive metastasized retroperitoneal tumors. *J Am M Ass* 933, 9 6
8. HART, W. Chorionepitheliom und Archheim-Zondeische Reaktion. *Zentralbl f Gynak* 930, 54 260
9. KAUFMANN, L. Intragenital chorionepithelioma in male. *Am J Path* 934, 10 443-448
10. KATZBERG, ROBERT A. } The value of hormonal  
study in the diagnosis of chorionepithelioma. *Am J Obst & Gynec* 934, 26 2-3
11. LAMM, M. and ELLIS, E. A report of cases of chorionepithelioma followed by the Friedman test. *Am J Obst & Gynec* 933, 3 906-907
12. LEVITZKY, MICHAEL L. and SUMER, WILLIAM. Chorionepithelioma. *J Am M Ass* 934, 3 668
13. LYNCH, F. A. and MAXWELL, A. P. *Pelvic Neoplasms*, p. 300. New York: D. Appleton & Co. 93
14. MACK, H. C. and CARRINGTON, A. E. Archheim-Zonde reaction in hydatidiform mole and malignant chorionepithelioma. *Am J Obst & Gynec* 930, 10 670
15. MATTHEW, E. Report of chorionepithelioma with defective pregnancy hypothesis. *Arch f Gynak* 933, 5 1
16. MATTHEW, E. and MCKENNA, T. The Archheim-Zonde pregnancy test. Analysis of one hundred fifty cases by simplified technique. *Northwest Med* 93 30 35
17. MATTHEW, A. PALMER, A. and HOLLAND, A. The Friedman pregnancy test. *Northwest Med* 93, 3 5
18. MATTHEW, C. and EISENBERG, L. Value of Archheim-Zonde reaction in diagnosis and prognosis of the chorionepithelioma. *Am J Obst & Gynec* 933, 10 95
19. MCNEILL, LYLE G. and RAYMOND, PHILIP A. The Friedman test for pregnancy. *Calif & Western Med* 933, 35 8
20. NEUMANN, H. O. Chorionepitheliom und Archheim-Zondeische Reaktion. *Zentralbl f Gynak* 93 44 448
21. PERAZICH, THOMAS C. Chorionepithelioma of the uterus. *Am J Obst & Gynec* 1934, 28 437-441
22. RILEY, E. Primary syncytoma of the ovary. *Am J Obst* 9 5, 7 46
23. ROBERTSON, W. The significance of the Archheim-Zonde reaction in the indications for treatment following hydatid mole. *Arch f Gynak* 1933, 19 317-320
24. ROEMER, H. and STROCKMANN, W. Ueber die diagnostische Bedeutung des Hypophysen-vorderlappen-hormons in Urin in Fällen von Blastozysten und Chorionepitheliom. *Zentralbl f Geburtsh u. Gynak* 930, 90 516
25. SA, P. Chorionepithelioma with positive results of Archheim-Zonde test. case. *Rev de gynec* d'obstet. 933, 37 306
26. SCHULTZ-KORNHUBER, F. Erfahrungen mit der Archheim-Zondeische Reaktion, besonders bei Mole gravidis und Chorionepithelioma. *Zentralbl f Gynak* 930, 54 578
27. SCHULTZ, H. (Graz). Zwei biologische Nachversuche reiner Chorionepitheliom, der Mole und des Chorionepithelioma, zu dem Harn-Hormon. *Nachsch. 91 44 1045*
28. STEIN, H. Primary chorionepithelioma of the uterus with report of case. *Am J Obst & Gynec* 934, 1 476

## HYPEROSTOSIS FRONTALIS INTERNA

## A PRELIMINARY STUDY

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THE term hyperostosis frontalis interna was chosen to designate a peculiar and striking condition occasionally found in the frontal bone and associated with various symptoms which will be described. When this title was selected the writer was ignorant of the thesis of Ferdinand Morel, "L'hyperostose frontale interne Syndrome de l'hyperostose frontale interne avec adipeuse et troubles cerebraux," published in 1930. It was only through search of the *Index Medicus* for the title "hyperostosis frontalis interna" or a similar one, that Morel's thesis was found. The name hyperostosis frontalis interna will be retained in this paper as it seems preferable to the French equivalent. However, there is no question as to priority in the selection of terms or presentation of the subject. To Ferdinand Morel all credit is due for his excellent study and the first report of a living example of the condition, which is to be discussed in this communication.

Radiological examination of the skull during some 10 or more years has on rare occa-

sions shown a peculiar thickening of the frontal bone. This thickening has been considered as either a normal anatomical variation, such as overdevelopment of the groove for the longitudinal sinus, or of bone formation, or calcification in the falx cerebri, or some indefinite type of osteitis. The patients in whom it has been found have not had pathological study of the area in question or examination at autopsy. Little attention was paid to it. Nevertheless, the finding seemed significant, and its occurrence was more carefully noted for some years. In 1929, an example of melorheostosis came under observation and it was thought that this condition in the frontal bone might be a cranial manifestation of that disease. From then onward the cases having this change were carefully noted in the hope that a sufficient number would be collected to warrant a study of what was thought to be melorheostosis of the cranial bones. The cases were too infrequent in occurrence to result in any progress. Consequently, it seemed advisable to re-examine all the radiographic mate-

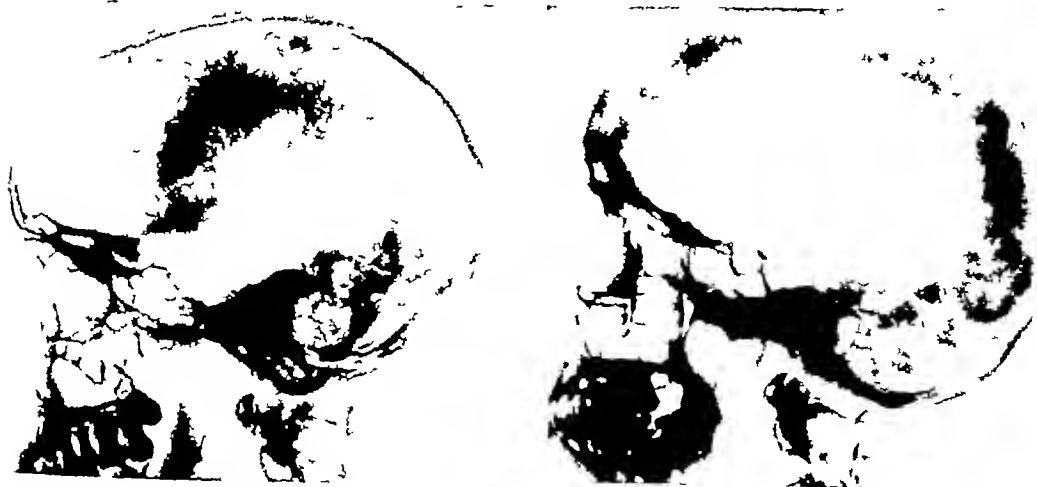


Fig 1 Lateral roentgenograms of skull of normal adult individuals. Left, male. Right, female.

TABLE L.—AGE SEX RACE

Age in years	Female		Male	
	White	Colored	White	Colored
14-20	250		277	21
20-30-40	26	25	491	26
40-50-60	51	6	527	21
60-70-80	173	61	499	54
90-100-110	268	27	579	26
120-130-140	1,000		77	
140-150-160	99		180	
160-170-180	75		26	
180-190-200				
Total	2,439	117	2,066	127
	Female—97% (White—95%)		Male—94% (White—92%)	

rial available. Before discussing the reexamination some remarks on the literature of the subject are in order.

The literature is fully covered by Morel and but brief reference will be made to it. His thesis, published in 1930 is based on 4 personal autopsies at the Bel-Air Asylum at Geneva, the protocols of 11 others and a study of a living case at the time of his writing an inmate of the asylum. In 1930, Van Bogaert reported a case. Le syndrome de l'hyperostose frontale interne chez une malade présentant par ailleurs un Cécité psychique par hémianopsie double and in 1931 P. Schiff and J. Trelles recorded an additional case under this title "Syndrome de Stewart Morel (Hyperostose frontale interne avec adipose et troubles mentaux)." As far as the writer is able to ascertain, these 3 cases are the only ones studied during life. However the clinical aspects and radiological findings are so characteristic and unique that the disorder must have been described more frequently. If so the reports are under titles difficult or impossible to find.

Hyperostosis of the frontal bone associated with obesity has been known in the autopsy room for an exceedingly long time. Morel relates the interesting fact that Morgagni and Santorini performed an autopsy on an old woman undoubtedly having hyperostosis frontalis interna, an observation published in 1765. Naito in his monograph *Die Hyperostosen des Schädels* includes the X-ray

Fig. Top, B. H. 3907 first degree. Middle, private case second degree. Below, O. P. D. 1,40730 third degree (made from an old and much faded glass plate).

examination of 9 skulls with hyperostosis, but little or no history Casati, in 1926, "Die senilen Schaedelveraenderungen im Roentgenbild," published radiographs of 5 examples of the condition found among museum specimens R M Stewart reported the autopsies of 3 personal cases and a study of certain museum specimens in 1928 under the title "Localized Cranial Hyperostosis in the Insane" D M Greig, in 1928, published an elaborate article "On Intracranial Osteophytes" His study was based on 188 crania in the Museum of the Royal College of Surgeons of Edinburgh Among them were 32 with "intracranial osteophytes," many of them identical with those of hyperostosis frontalis interna An interesting point is the fact that he states that the orbital portion of the frontal bone is free from the hyperostosis

The radiographic material studied was that in the file of the Edward Mallinckrodt Institute of Radiology which also contains the X-ray negatives of its predecessor the X-ray Department of the Washington University School of Medicine The roentgenograms were accumulated from September, 1911, to May, 1934 During that period there were 288,860 admissions to the Washington University Dispensary and its successor, the Washington University Clinics There were, in the same period, 127,084 admissions to the hospitals allied to the Washington University School of Medicine, namely, the Barnes, the St Louis Children's, the St Louis Maternity, and the McMillan Eye, Ear, Nose and Throat Hospitals The total number of patients applying to these institutions was 415,944 and roentgen examinations were made on 96,076 of them Of these 5,955 were of the skull (Table I)

In the interest of accuracy and because the particular frontal bone change was either not noted or, if noted done so under innumerable designations or synonymous terms it was essential to review all X-ray negatives of the skull, from 15,000 to 20,000 in number To insure complete mental detachment and to make the survey wholly objective in character the plates and films were examined to determine whether or not there was deviation from the roentgenographic



Fig 3 B H 34347 Above, nodular type of hyperostosis B H 173338 Below, sessile type of hyperostosis

findings of a normal individual (Fig 1) There was no prior knowledge of the history of the case reason for the examination, or other facts concerning the patients The negatives were reviewed in the order in which they were made This method was essential for elimination of the natural tendency to find in an X-ray examination that which symptoms, physical examination or other facts indicate should be present

Practically all roentgenographic examinations of the skull were made stereoscopically in the lateral projection Many had in addition a postero-anterior projection and many

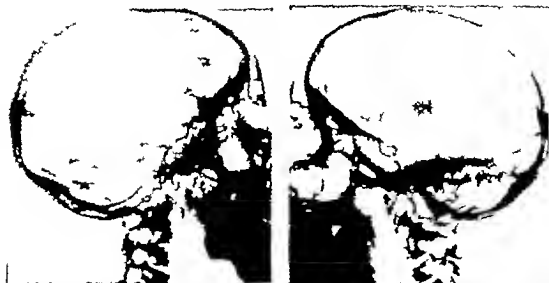


Fig 4. B. H. 9330. Left, involvement of orbital plate and sphenoid portion of the frontal bone. Right, B. H. 979, orbital plate alone involved.

of the latter were also stereoscopic. Because of inefficient apparatus, poor technique, and the effects of time, many of the earlier plates and films had to be eliminated from consideration. If roentgenograms of other regions of the body had also been made, those were examined to ascertain if there were bone changes elsewhere. No such changes were discovered.

Seventy-two examples of frontal bone hyperostosis were found. They varied in degree from those in which the change was detectable to extreme thickness. It was impossible to consider the variation in thickness and density in relation to the time of existence of the bone change. The examples are divided into three classes, first, second, and third degree in ascending order (Fig 3). They are of three types, nodular, scudle, and mixed (Fig 3).

Regionally the hyperostosis can be classified into that in which it is confined to the squamous portion of the frontal bone, to its orbital plate, and to a combination of the two (Fig 4). The hyperostosis was associated in a few cases with hyperostosis elsewhere in the vault of the skull, notably an indefinite thickening of the frontal bone near the coronal suture lateral to the sagittal plane.

The hyperostosis is of a dense order, the density being disproportionate to that which could be ascribed to the increased volume of the involved portion of the bone. Though it may extend far up on the squama, it is not observed beyond the coronal suture. The frontal sinus may have its posterior wall thickened on the cranial aspect but the cavity is not decreased.

There is no evidence of hyperostosis of the sphenoid, temporal, or malar bones. The cribriform plate of the ethmoid is scarcely or not at all possible of roentgenographic examination, hence no statement regarding it can be made. It is to be remembered that the ethmoid is developed in cartilage, whereas the frontal is a membranous bone. The lateral extent of the hyperostosis is not determined even in the postero-anterior view. This region cannot be investigated with certainty by roentgenography because of superimposition of too many structures in the postero-anterior projection and the backward curvature of the lateral portion of the squama frontalis. The hyperostotic change gradually fades from the midline laterally. At the midline there is a narrow zone in which the hyperostosis is non-existent, or is present to only a slight degree. In the living subject the thickness of the



Fig 5 B H 2788 First degree hyperostosis Photograph illustrating obesity

hyperostotic area can only be estimated in roentgenograms made in the lateral projection

Schueller writes that "apart from variations in thickness in separate skull regions the average thickness of the skulls of different adults varies between 3 to 8 millimeters." Table II is an attempt at measurement of the hyperostotic areas; they were made at the extreme point of thickening. It must be remembered, however, that these are measurements of roentgenograms which are made at a point on the sagittal plane and outward over a curved surface and that they are of relative value only.

In no case was there any evidence of alteration of the outer table of the skull. The diploe, according to the degree of hyperostosis, is either diminished or obliterated, and this appears to be progressive. When the thickening reaches the inner aspect of the outer table, its progress is arrested and in such cases there is radiographically a homogeneous mass of dense bone extending from the outer surface of the skull to the inner limits of the hyperostotic zone. In the cases in which the orbital plate is involved, there is, of course, no replacement of diploe by compact bone, because the orbital plate is papyraceous. Toward the cranial cavity, the hyperostosis extends, in the most extreme case in the

material which was studied 46 millimeters from the outer surface of the cranium (see Fig 2). The zones of hyperostosis are wavy in their intracranial outline in the nodular and smooth in the sessile type, and are homogeneous in texture. There are no signs of bone destruction or calcium loss. In all cases, the skull was free from evidence of increased porosity with one exception (B H 24503). Since the hyperostotic area is radiographically, at least, formed of a mass of dense bone, it is necessary to compare it with the hyperostosis or hypertrophy which are to be observed in other bone dystrophies.

Through its physical characteristics, location, and incidence, this hyperostosis is distinct from that observed in the infectious processes of bone, primary or secondary bone tumor, osteitis deformans, melorheostosis and leontiasis ossea. It obviously should not be confused with those bone dystrophies in which porosity or calcium loss is a feature. It lacks all the characteristics of the bone changes observed in the blood dyscrasias.

Hyperostosis frontalis interna is the antithesis of those diseases which have a deficiency of skeletal calcium as a part of their picture. It is, therefore, a reasonable supposition that it is a disorder of calcium metabolism<sup>1</sup> in

<sup>1</sup> The term calcium metabolism will be used throughout this paper. It is to be understood that the term includes all related metabolites.



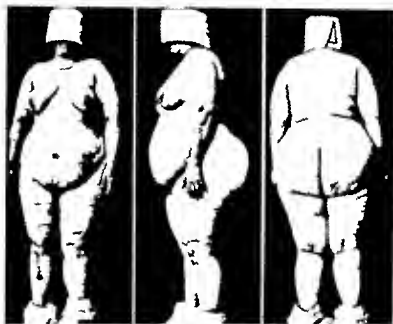


Fig 6 B H 457 Illustrating obesity

which that mineral is present in excess in the organism Greig and Morel are of this opinion. There is associated a disturbance of fat metabolism manifested as obesity which is at times extreme (Figs 5 6 and 7). The occurrence of the latter is less constant than the calcium disorder as it is seen in but 44 per cent of the cases.

The incidence of hyperostosis frontalis interna will vary with various types of institutions. In a general hospital and dispensary in a period of 23 years there were 59 examples in 415 944 patients, a percentage of .014. In an X-ray laboratory 72 cases were found in 96 076 examinations a percentage of .075. On roentgenographic examination of the skull alone there were 72 examples in 5 955 cases or 1.2 per cent. At the Bel Air Asylum in Geneva Morel found the incidence to be 1.4 per cent of the autopsies. Regardless of these percentages it is a fact that the actual incidence must be higher than the figures mentioned, certainly it will be found so if the condition is sought for. The surest means of determining the existence of the hyperostosis is by radiographic examination. Certain

degrees or types of hyperostosis may readily escape notice at autopsy.

After segregation and analysis of the roentgenographic material the 59 cases in which a clinical history was available were analyzed. The case histories were reviewed in the same manner as were the examinations of the skull, that is, as far as was possible under the circumstances, with complete detachment. No reference was made to the radiographic findings and only the salient points in the histories were noted or that which appeared to be of importance to the writer of the clinical record.

Analysis and tabulation of these facts in the histories are immediately arresting and are as striking as were the results of the review of the roentgenograms (Table III). The important features in the table may be summarized as follows. With two exceptions (B H 25796 and B H 26766) which were acute traumatic cases, 70 patients had neurological or neuropsychiatric symptoms of an intensity requiring a roentgenographic examination of the skull. Fifty-five or 76 per cent, of the 72 cases were hospitalized 97.2 per cent were females. Of

those 59 with histories available only 50.8 per cent had been pregnant (from 1 to 21 times), 3.4 per cent had a positive Wassermann. The ratio of colored to white patients was approximately the same as that prevailing in this clinic, 62.7 per cent had headache, 5.08 per cent migraine. 8.5 per cent had convulsions, 4.4 per cent were obese, and 5 per cent had thyroid disorder. There is some justifiable doubt as to the two male cases being true examples of the disorder (Fig 8). The incidence by decades is shown in Table IV.

There are certain impressions gained from the tabulation of the histories which cannot be put down in figures. The majority of the patients gave a long history of morbidity which is quite indefinite. There is no evidence that pregnancy or barrenness has any relationship to the condition. The reading of the histories of these cases individually leaves an impression of vagueness, the symptoms related or the physical examination do not fit with any particular pathological state or they might be a part of many diseases. Taken *en masse*, however, they constitute a definite syndrome which is distinctive. Polyphagia, polydipsia, polyuria, and disturbance of sleep emphasized as important symptoms by Morel were not recorded in 59 of the cases. Possibly these symptoms were so slight that they escaped notice.

If on X-ray examination of the skull, hyperostosis of the frontal bone is encountered, it is the most certain sign of the existence of this disorder, and one is tempted to refer to it as a "pathonomonic" sign. If



Fig 7 Same patient as in Figure 6. Above, roentgenogram of skull in 1924. Below, roentgenogram of skull made in 1934. There is a question of slight enlargement of the sella turcica.



Fig 8 Roentgenograms of the two male cases.



Fig 9 B H 807 Left, lateral roentgenogram Right, postero anterior roentgenogram of skull

coupled with hyperostosis there is a tendency to obesity various bizarre mental and neurological symptoms and signs, the diagnosis of the condition is established. In addition to this, the degree of the hyperostosis seems to be in relation to the intensity of the symptoms and both the hyperostosis and the symptoms appear to be of a progressive nature. There must be a single fundamental cause which produces both the hyperostosis and the symptoms from which the patients suffer in the beginning. At a later period if the hyperostosis is of such an order that the

cranial contents are encroached upon by bony overgrowth, there are superadded other symptoms which are not to be confused with those traceable to the unknown fundamental causative factor. To illustrate, autopsy reports in the extreme degrees of hyperostosis mention the fact that the frontal lobes conform or are molded to the hyperostotic zone. This can only mean that the brain atrophies before the advance of the encroaching bone. Naturally in such cases what is being dealt with is cerebral pressure analogous to that of a long standing depressed fracture of the skull.



Fig 10 B H 8230 The thickened orbital plate shown in left lateral roentgenogram Right, postero-anterior projection. Not crowding of left orbit in postero anterior view

There have been no convincing roentgenograms which demonstrate hyperostosis throughout the base of the skull except in the case of the orbital plate of the frontal bone. Nevertheless, the high incidence of seventh and eighth nerve symptoms, strongly suggest that hyperostosis of the temporal bone may be the cause of the symptoms, frequently found, referable to these nerves. Morel's case (Case No 11) had isolated hyperostoses on the petrous portion of the temporal bone.

It is impossible to understand why there is a selectivity of location of this hyperostosis. The assumption that there is a selectivity must be provisional until it has been established by autopsy and roentgenography that there is no accompanying hyperostosis of the other portions of the skeleton. Greig's view is that the senile skeleton (the average age of his cases was 70 years) because of general inactivity of elderly individuals, loses its calcium to the blood stream. In consequence of this there is calcium retention which is deposited somewhere in the organism. In the case of the frontal bone the cerebral atrophy, incident to old age, results in traction on the dura mater which brings about negative pressure between dura and inner table. This negative pressure is dominant in the case of the frontal bone because of the firm dural attachments on that bone coupled with the time spent in the dorsal decubitus by elderly persons. This explanation ignores the question of osmosis which would be brought into operation by negative pressure. The dura is more closely attached to the frontal bone than elsewhere in the cranium, in fact so adherent in hyperostosis that at times it cannot be loosened. Morel believes that the membrane contracts along the course of its fibers and that these are the lines of force which produce the irregular inner surface of the hyperostosis. In this Morel seems not to have encountered the sessile or flat type of hyperostosis. The existence of the flat type destroys his most ingenious theory. He also is of the opinion that the dorsal decubitus of the elderly, contributes in part to the production of the hyperostosis. An older and long held theory as to the causation of the hyperostosis, was that it was a compensatory process for filling the

space produced by atrophy of the frontal lobes of the brain. Neither Greig nor Morel subscribe to this theory.

Both Greig and Morel, if they are understood correctly, consider that the hyperostosis extends from the surface of the inner table into the cranial cavity only. As far as it can be determined by roentgenography the series of cases comprising this report indicate that the dense hyperostosis progresses in both directions as has been pointed out above. Figures 3 and 4 (roentgenograms) in Morel's (loc cit) monograph clearly show dense bone in the diploic space.

Greig states that the hyperostosis is made up of cancellous bone with its intracranial aspect covered by a lamina of compact bone and he leaves one under the impression that he considers this cancellous bone as identical with that of the diploic space. Roentgenographically it is not identical, being much denser than the remainder of the diploe, in fact, it has the physical characteristics of compact bone. On the other hand, however, if on gross and microscopic section the hyperostotic bone is actually cancellous, then the evidence is that the bone trabeculae contain a far greater amount of calcium than is normally the case and there is a hypercalcinos of the diploe.

Morel insists that the hyperostosis is confined to the two halves of the vertical portion of the frontal bone (Fig 9) and makes no mention of hyperostosis of the orbital plates of that bone (Fig 10). Figure 4 illustrates an hyperostosis both alone and combined with involvement of the squama.

Up to quite recently on the rare occasions when this hyperostosis has been noted, it has been thought to be an incidental finding in the autopsy of aged insane persons, usually females. Greig considers the hyperostosis of no clinical moment and maintains that it is compatible with a long and active life. Certainly his material indicates that it does not affect longevity. It must be remembered, however, that his examples consisted of museum specimens, and such notes as he had on the individuals would necessarily be limited in scope, certainly too limited to permit him to consider the hyperostosis as only an involuntary change incidental to old age. He also

TABLE II.—DEGREE AND TYPE OF HYPEROSTOSIS

Temp No	Degree	Molecular	Crystals	Thickness in millimeters				Other skull hyperostosis
				Lower table	Outer table	Traces	Osteal plate	
B H 1788				Total—1				
B H 1799								
B H 2600				Total—2				Diffuse hyperostosis of calvarium
B H 11343				1				
B H 11181							2+	
B H 2602				Total—12				Hairpins over right orbit—P A view
B H 1432				Total—17				
B H 1730				1		Traces		Posterior wall frontal sinus—4 mm.
B H 1304				Total—13				Posterior wall frontal sinus—4 mm.
B H 18041				12		17	3	Posterior wall frontal sinus—4 mm.
B H 26394				Not measurable				
B H 17111				Total—1				
B H 17540				20	1+	Traces		Endosteum gone. Softs enlarged.
B H 18086				14		17		Posterior wall frontal sinus—4 mm.
B H 13030								
B H 17701				1			1	
B H 19020				Total—13				Thick
B H 19077				Total—9				Paranasal hyperostosis
B H 2604				Total—9				Posterior wall frontal sinus—4 mm.
B H 1891				20				Posterior wall frontal sinus—4 mm.
B H 16305				Total—13				Large calcification of inferior orbital post-orbital. Posterior wall frontal sinus—4 mm. Oculopharyngeal Atrophy
B H 16011				20			1	
B H 17090				1	+	1		Calvarium thickened—4 cm.
B H 16700				Total—11				Posterior wall frontal sinus sinus
B H 16004				Total—14				
B H 17303				Total—12				Osteal hyperostosis of calvarium
B H 17130				20				Slight paranasal hyperostosis
B H 1691				20				
B H 19170				1	17			Posterior wall frontal sinus—4 mm.
B H 2001				Total—15				Anterior wall frontal sinus thick. Hyperostosis elsewhere
B H 20015				Total—11				Thick skull
B H 21177					2+			
B H 21177				Not measurable				
B H 15794						+		
B H 23001								
B H 26007				Total—10				
B H 201				1			Thick	Diffuse hyperostosis of calvarium. Destruction of pulp
B H 27704				Not measurable				
B H 26000				Total—17				
B H 201				Total—16				
B H 20019				Total—1				Thick
B H 21121				10		1		Posterior wall frontal sinus sinus. Quaternary evidence

TABLE II—DEGREE AND TYPE OF HYPEROSTOSIS—Concluded

Hosp No	Degree	Nodular	Ses ile	Thickness in millimeters				Other skull hyperostoses
				Inner table	Outer table	Diploe	Orbital plate	
B.H. 34180	1			14	1			Large sphenoparietal sinus
B.H. 14394	1			8	2	2		
B.H. 16043	3			Total—13			5	
B.H. 17333	1			8	2	3		General hyperostosis. Bridged sella
B.H. 18072	3			11	-	Trace	4	Posterior wall frontal sinus—5 mm.
B.H. 18091	3			Total—3				
B.H. 18334	1?			6	1	3		
B.H. 19456	1			9	1	Trace		Posterior wall frontal sinus—6 mm.
B.H. 21532	2			17	1	2		
B.H. 24172	1?			Not measurable				General bone atrophy. Acromegalic type
B.H. 41053	2			14	2	3		
B.H. 42666	1			Not measurable				Cranium thin
B.H. 42710	24 1 34 2			13 10	3	Trace		
O.P.D. C3194	3			Total—19				
O.P.D. C12743	2			Total—15			4	Posterior wall frontal sinus—7 mm.
O.P.D. C50456	3			Total—46			10	General hyperostosis. Posterior wall frontal sinus thick. Parietal—10 mm.
O.P.D. B74454	2			Total—15				Posterior wall frontal sinus thick
M.S. Pvt.	1			5	1	3		
T.S. Pvt.	1			8	-	4		
B.S. Pvt.	1			Total—14			5	Posterior wall frontal sinus—7 mm.
H.S. Pvt.	2	Mixed		7	3	-		
D.S. Pvt.	1			6	2	1		
J.S. Pvt.	1				3			Hyperostotic area—12 mm. Destruction of sella
R.M. Pvt.	1?			Total—11				Thin skull
E.H. Pvt.	2			5	1	3		Large bilateral sphenoidal sinus
V.D. Pvt.	2			Total—13			6	
M.B. Pvt.	2			9	2	3		
L.M. Pvt.	1			4	1+	3		
R.H. Pvt.	2			Total—13				Ossification of falx
M.C. Pvt.	2			12	2	4		

appears to ignore the fact that 28 of his 32 patients, or 87.5 per cent, were women. All of the cases of Stewart, Morel, and Naito, were insane though they were all of an advanced age. The cases of Van Bogaert and Schiff and Trelles of less advanced years were of such severity as practically to disable the patients. It is apparent that in its full development this syndrome is associated with psychosis. Seventy of the 72 cases comprising this study were all of a degree of morbidity

calling for medical and, in 55 cases, hospital care. The study of their clinical histories is convincing proof of their invalidism. The average age 44 years the degree of hyperostosis and the intensity of the accompanying symptoms were less than those of Morel and Stewart. The study of the 70 cases suggests that there is progression of the disease which may reach the extreme seen in the maternal Stewart and Morel have reported in the literature.

TABLE III

Case No.	Age last	Race	Progression	Entered hospital for	Complications	Diagnosis	Metabolic disease	On eye	Remarks
B. H. 5763	34	W	none	Ophthalmic pain Sclerotic weakness	Lumbar arthritis	+	Obese		Fatigue
B. H. 5769	34	W		Diabetes	Optic-arthropathy Hypertension	-			Psychasthenia
B. H. 5868	34	W	4	Frontal headache	Tumor of brain nasal	-	Obese		
B. H. 71343	34	W		Edema of legs. Excretion Multiple of conditions	Hypertension No psychomotor	-	Obese		
B. H. 761	34	W		Sudden loss of vision, rt. eye 12, eye blind	Hypertension Toxin hemorrhoid on leg	-	Obese		Weakness. Cerebral nerve degeneration
B. H. 5614	34	W		Diphtheria, eye. Speech difficulty	Thyroidectomy	-			Mentally dull
B. H. 7434	34	W		Pain in eye and head. Swelling of lids	Menstrual hyperemia nasal	-	Obese Diabetes		1
B. H. 4139	34	W	none	Headache	Appendicitis Venous hypertension	-			
B. H. 15565	34	W	none	Headache. Convulsions	Hydrocephalus	-	Obese		Small defect
B. H. 5644	34	W		Asthma, eye. Pain eye R eye. Headache	Hypertension	-			Vision mentally hyper. difficulty
B. H. 18776	34	W	1		Cataracts	-			
B. H. 57501	34	W		Headache. Puffed vision. Double	Subconjunctival dema	-			Cerebral degeneration 1st nerve
B. H. 17748	34	W		Headache. Puffed vision. Mentally dull	Exophthalmic crisis vision negative	-	Obese		Ringing in ears Mentally dull
B. H. 5646	34	W	none	Headache. Arthritis. Lumbar	Hypertension Hypertension	-			Morose. Pachyma 1st nerve
B. H. 59010	34	W		Headache. accepted vision		-			Petechiae. Embolism
B. H. 6794	34	Col	none	Headache. accepted along vision	Conjunctivitis. skull abnormal. U7	+			Weakness. Tremor
B. H. 59906	34	W		Headache. double diphtheria. Various nasal					4th nerve weakness
B. H. 59777	34	W	none	Jacksonian epilepsy years					
B. H. 57666	34	W		Tremor. multiple (1st. Lumbar. Vision fading vision. Short nose of brain)	Glaucoma Exophthalm. Op	-			Rt. Sacral weakness. Ringing in ears. Lumbar
B. H. 11995	34	Col		Headache. Pain behind left eye		-			Pain vision Myopia. Spasmodic movements of face and hand
B. H. 54303	34	W	none	Headache. Pain vision, R eye. Arthritis	Old cystitis prostate. Duet 4. on yrs.				Irritability. Weakness
B. H. 64511	34	W		Hypochondriac. Head ache. Double, dull	Head injury accident				Morose. Tremor. Ringing in ears
B. H. 17796	34	W		Tremor. cost	excess of chloride				
B. H. 59-64	34	W		Tremor. cost					Hysteria
B. H. 5964	34	W		Epilepsy. grand and petit. many years					
B. H. 57592	34	W		Fatigability	Hypertension		Obese		

TABLE III—Continued

No	P No	Age Sex	Race	Pregnancies	Entered hospital for	Complications	Serology	Metabolic disease	De gree	Neurologic
BH	27450	52 F	Col.	1	Diabetes			Obese	1	
BH	9511	44 F	Col	21	Headache frontal Pan. aneurysm	Osteomyelitis frontal bone?	—		2	
B.H.	950	33 F	W	none	Headache severe, 6 mos. Bilateral choked discs	Op chr left mastoiditis	—		1	
BH	30163	51 F	W	6	Obesity Allergy	Dermatitis. Hypertension	—	Obese	2	
B.H	321	62 F	W	2	Headache occipital frequent with vomiting	Arteriosclerosis Chondrotyphus fetalis	—	Obese	1	Rt. 7th paralysis Mentally dull
B.H	30183	43 F	W		Headache occipital and parietal severe Un steady gait		—		1	Progressive weakness?
B.H.	34347	40 F	W	4	Psychoneurosis Failing vision 3 yrs		—	Obese	2	Nervous
B.H	3564	35 F	W		Headache Fatigue Brain tumor suspect	Sinusitis 4 years	—		1	Dizziness Blurring left eye. Tickling of tongue
B.H.	35993	28 F	W		Migraine Severe head ache 25 years Allergy	Sphenoidal sinusitis	—		1	Fatigue Talkative Querulous Cranial nerves negative
B.H	36667	42 F	W		Epileptic attack 18 mos previously		—	Obese	1	Nervousness
B.H	37551	64 F	W		Headache frontal 8 mos	Arteriosclerosis	—	Obese	2	Nervousness
B.H	3764	50 F	W	4	Arthritis deformans	Chr sinusitis	—	Obese	3	
B.H	38108	60 F	W		Arteriosclerosis. Myopia. Sl deaf Headache	Sinus op Hypertension	—	Obese	2	Nervous Eyes prominent. Fibro- blastoma 8th nerve
B.H	39113	56 F	W		Headaches 2 yrs Nervousness	Craniotomy Fibroblastoma 8th nerve	—		2	
B.H	41822	54 F	W	2	Headache Petit mal at 5	Consulated EENT	—		1	
B.H.	39110	48 F	W	4	Dim vision 3 yrs Arteriosclerosis		—	Obese	1	Mentally dull Unable to write at times
B.H.	34180	50 F	W	4	Staggering gait. Poor memory Falling to rt and left	Possible cerebral arteriosclerosis	—		1	Tinnitus. Dim vision Impaired hearing
BH	14894	65 F	W	2	Neuralgia 5th nerve Dim vision	Mastoid op	—	Obese	3	Numbness lt. arm. Tingling and crawl- ing sensation of scalp and lt. leg
B.H	16013	38 F	W	1	Tumor of brain suspect uncertified Headache occipital 3 mos	Accident 3 yrs ago, no symptoms until 1 yr ago	—		1	Nervous. Irritable
BH	17338	31 F	Col		Neurosis Dragging lt. leg	Myoma uterus	—		1	Numbness weakness. Bilateral Babinski
B.H.	18072	35 F	Col	5	Tbc. 4th dorsal vertebra Paraplegia	Chr cystitis	—	Obese	3	Dizziness
B.H.	18091	40 F	W	9	Headache, occipital and frontal with nausea and vomiting. Dizziness 20 years Arthritis Dyspepsia	Osteoarthritis Chr cholecystitis	—		1	Nervousness. Fatigue
B.H	18884	54 M	Col		Steady headache 5 yrs. Vertigo Nervousness	Osteoma left tempur Chr sphenoiditis operation	—	Obese	1	
BH	19456	72 F	W	2	Headache. Hemiplegia. Vertigo Vomiting		—	Obese	1	



TABLE III—Carcinoid

Case No.	Age	Sex	Findings	Extant hospital for	Complications	Roentgen	Myeloid disease	Drugs	Remarks
B.H. 11283	1	Col	none	Headache, 7th cranial nerve paralysis	Meningeal fibrosarcoma	—	—	—	Fading sensory Nervousness
B.H. 8417	17	W	1	Headache, frontal and occipital, bilateral hemianopia	Craniospinal cysticary	—	Obese	—	Fading vision
B.H. 1493	17	W	—	Headache, frontal, 7th nerve as 1 vomiting Fading vision Tumor of brain suspected	—	—	—	—	7th nerve weakness
B.H. 12646	1	W	—	Headache, severe Migraine (severe) large left eye Double vision	—	—	—	—	—
B.H. 47146	1	W	—	Headache, severe 11th nerve (severe) Anisocoria	Primary tumor 1	—	Obese	1/2 11	—
OPD C3494	17	W	—	Headache, double Migraine Migraine, 11	—	—	—	—	Bottom Post sensory
OPD C417	17	W	—	Headache, Double, 7th cranial nerve in 11	—	—	Obese	—	Fading Double vision
OPD C2076	1	Col	—	Headache, frontal, not checked	—	—	Obese	—	Frontal Worry
OPD B1414	1	W	—	Headache	Chronic meningitis	—	—	—	—
M.S. Pnt	1	W	—	History unobtainable	—	—	—	—	—
T.S. Pnt	1	W	—	History unobtainable	—	—	—	—	—
B.S. Pnt	1	W	—	History unobtainable	—	—	—	—	—
H.S. Pnt	1	Col	—	History unobtainable	—	—	—	—	—
D.S. Pnt	1	W	—	History unobtainable	—	—	—	—	—
J.S. Pnt	1	W	—	History unobtainable	—	—	—	—	—
B.W. Pnt	1	W	—	History unobtainable	—	—	—	—	—
E.H. Pnt	17	W	—	History unobtainable	—	—	—	—	—
D. Pnt	1	W	—	History unobtainable	—	—	—	—	—
M.B. Pnt	1	W	—	History unobtainable	—	—	—	—	—
J.M. Pnt	1	W	—	History unobtainable	—	—	—	—	—
R.N. Pnt	1	W	—	Fatigue depressed	—	—	Obese	—	Fatigue depressed
M.C. Pnt	1	W	—	Recurrent headache	—	—	—	—	—

Cysticary: Craniospinal

Anisocoria: Acute meningitis

Cysticary: Migraine: Meningeal fibrosarcoma: craniospinal cystic

Cysticary: Migraine: Meningeal fibrosarcoma

Cysticary: Meningeal fibrosarcoma: tumor of hypothalamic region

At relapsing case was 8 years of age and had been confined to the asylum for 30 years. The roentgenograms of the skull show a pronounced degree of internal hyperostosis. It

can be taken as an example of this disorder in its complete form. Van Bogaert's case was a female aged 66 years with progressive mental deterioration and obesity. There is also

the interesting fact that her blindness was attributable to disturbance in the visual center and presumptive pressure on the optic nerve in the orbital foramen. This latter finding is of the first importance. The case of Schiff and Trelles was a male, aged 60 years. Following an accident with concussion of the brain the patient had headache, convulsions, and personality change. There was disturbance of gait and equilibrium and a negative Wassermann. Roentgenography revealed a typical internal frontal hyperostosis. Schiff and Trelles summarized the findings in their patient as follows:

- "A psychic syndrome characterized by
- Intellectual slowness, depression, and anxiety,
  - Disturbance of temperament and of character,
  - Protective neurosis

Neurological syndrome—

- Continuous headache with paroxysmal exacerbations,
- Difficulty in gait and equilibrium,
- Obesity of the hypophyseal genital type, extreme

Changes in the serum balance—

- Hypercalcemia
- Deficiency in the hydrogen-ion concentrations in the direction of an acidosis without change in the alkaline reserve "

In the 7 autopsy reports, 3 by Stewart and 4 by Morel, the patients were generally obese and there was frequently a fatty infiltration of the skeletal muscles. Arterial calcification and arthritis appear to be no more frequent than would be the case in persons of like age. Except for the hyperostosis of the skull there is no mention of any particular bone change. However, bone changes have not been sought for systematically either at autopsy or, what would be a surer method, roentgenographically. In Stewart's cases there was a disappearance of the cellular elements in the pituitary with replacement by fibrous tissue. He considered the changes as of little consequence and as being approximately those to be anticipated in old people. The dura mater is reported as being intimately attached to the hyperostotic zones by Stewart, Morel, and Greig, and all signs of inflammation of this membrane and

TABLE IV —INCIDENCE BY DECADES

1	2	3	4	5	6	7	8
0	2	11	15	16	20	5	3

the underlying bone, past or present, are lacking. The surface of the bone is smooth. Both Morel and Greig write that there is no hyperostosis of the base of the skull. To digress at this point—It must be pointed out that hyperostosis in that location might easily escape observation at autopsy, whereas it could be readily discovered roentgenographically.

In 4 of his cases, Morel made serial sections of the third ventricle from a point just in front of the anterior commissure to the mamillary bodies. There were cellular lesions in the wall of the third ventricle which were sharp. They consisted of an excess of pigment and fat in the cells producing a granular appearance almost to the point of cellular disappearance. His conclusion is that there is present in hyperostosis frontalis interna a lesion in the wall of the third ventricle and that the cause of the lesion is also the cause of the syndrome. It is significant also that Case B H 24172 had a questionable solid tumor of the hypothalamic region. Stewart's pathological material excludes the pituitary as having any part in this disorder with some question as to its posterior lobe.

Since in this series of cases, 97.2 per cent are females and the average sex incidence of the cases reported by Naito, Stewart, Greig, Morel, Van Bogaert, Schiff, and Trelles is 82 per cent females, it is clear that the disorder is one so dominantly found in the female that differential diagnosis does not have to be concerned with those disorders which affect the sexes equally. This at once rules out any possibility of its being traceable to a deficiency disease. It likewise removes it from the class of such endocrine disturbances as have an equal or even nearly equal incidence in the two sexes. The evidence all points to the disease being one referable to some structure peculiar to the female. With the tabulation of the pregnancies given here it is difficult to see how this disorder can be attributed to the ovary.

It is self-evident that there is a mechanism common to both sexes for the control of calcium metabolism. Because of the functions of the female, which are related to calcium metabolism, it seems almost inescapable that the sex has a special mechanism for its control. Since hyperostosis frontalis interna occurs almost exclusively in women, it is proposed that there is a special structure present in the female which governs the calcium metabolism essential for menstruation, gestation and lactation. These three functions require the assimilation and disposal of an enormous amount of calcium and the requirements are intermittent. Now if such a theoretical mechanism should not undergo involution in step with that of the sex organs of the female of known function there might result an aberration in calcium metabolism. This appears to take place in hyperostosis frontalis interna, the deviation from normal being the retention of calcium which should be eliminated. The involution of such a calcium control mechanism should be greater with advance in years. In this condition, however involution is not in equilibrium with that of ovary, uterus, and breast. It may be that it is precocious, and hyperostosis frontalis interna a manifestation of premature old age. There is a strong temptation to draw an analogy between hyperostosis frontalis interna and chronic cystic mastitis. The material of this study however indicates that it is by no means confined to elderly persons but merely that it is more likely to be found in its extreme form in old age. However this theory may be it is certain that there is a disorder of calcium metabolism found in women and, despite clinical reports which are few in number only questionably occurring in the male. Alford's pathological findings are very suggestive in implicating the third ventricle as the locus of this theoretical mechanism.

Little is to be said as to prognosis until this syndrome has received much more study than it has, and its true nature is better understood. Until then the prognosis, certainly in a proportion of cases, is progressive nervous and mental deterioration and a terminal insanity in the extreme cases and long continued morbidity in those less pronounced. Perhaps

therapeutic indications may modify the prognosis.

It is fortunate indeed, that in this condition there are certain clear cut therapeutic indications. Before considering them thought is to be given certain diagnostic steps which should be taken in every suspected case. These are a painstaking analysis of the subjective history and of the symptoms, especially those of the cranial nerves. Study of the calcium-phosphorus metabolism and the acid base equilibrium of the blood serum should be done. The case of Schiff and Trefles emphasizes the necessity for this. Roentgenologically the examination should be more comprehensive than has been the case. This undoubtedly applies to the material in this study. There should be as a minimum a stereoscopic examination in the lateral projections from both sides of the skull, a stereoscopic examination in the postero-anterior projection, and an examination of the optic foramina, the latter is mandatory in cases such as that of Van Bogaert, as it is indeed in all cases. Until encephalography has been proved a useless procedure it should be carried out as a routine measure when there is a suspicion of any form of intracranial hyperostosis.

If metabolic studies reveal a faulty calcium-phosphorus balance or a disturbance of the acid base equilibrium then dietary experiments should be tried for the purpose of restoring metabolic balance. The use of parathyroid hormone appears to be distinctly worth a trial, as does a rachitic diet to counteract excessive calcium deposit. A digression is in order at this point. Negative findings in a single chemical examination of the blood for calcium content cannot be taken as indicating a normal condition. Detecting a slight hypercalcemia is difficult and success in finding it must be so to speak, accurately timed with the height of the changes which produces the hypercalcemia. Now if hyperostosis frontalis interna is the result of hypercalcemia, let it be remembered that this disorder is one of slow progression and there might be periods of arrest and possibly of remission further at no time would there be an extreme hypercalcemia.

If there are signs of increased intracranial pressure as a result of hyperostosis, on theoretical grounds, surgical intervention promises much. Indeed, exploratory operation of the frontal area is indicated in the absence of increased intracranial pressure if the symptoms accompanying hyperostosis frontalis interna are of a severity to warrant major steps. Unquestionably, Jacksonian episodes (not infrequent) in conjunction with a frontal hyperostosis are an operative indication. Compression of the optic nerves and this should be ascertainable at all times by roentgenographic methods, calls for surgical interference along the optic groove in those cases in which there is a hyperostosis of the orbital plate of the frontal bone. Massive projections of bone extending into the cranial cavity such as case O P D C50756 (see Fig. 2) certainly seems to call for removal as clearly as would a depressed fracture encroaching to this degree on the substance of the brain. Atrophy of the cerebral cortex beneath the nodulations of hyperostosis frontalis interna is reported. Because this atrophy is found in a "silent area," it does not follow that such nodulations are harmless. With the little knowledge there is regarding these "silent areas" it is unjustifiable not to deal with them just as would be done with an hyperostosis occurring in a region of the brain where focal symptoms result.

There are certain points that have been discovered at autopsy in this condition which are surgically suggestive. The first of these is that the groove for the longitudinal sinus does not share in the bony thickening. The other is that the outer layer of the dura is intimately attached to the bone, and this point is emphasized by all of the authors who have written on the subject. From their descriptions, this attachment seems to be so firm that it would be impossible to elevate the bone without rupture of the dura.

It has been mentioned that if the optic nerves are jeopardized by local pressure this constitutes a surgical indication for intervention. Though it has not been mentioned by others and was not found in the clinical analysis in the cases of this report it is possible that the olfactory nerve might also be-

come so strangulated as to give rise to important symptoms. The fact that this nerve penetrates a bone pre-formed in cartilage has been noted above. It also should be remembered that its exit from the cranium is near the midline, which region, at least in the case of the vertical portion of the frontal bone, is free from the hyperostosis, and the cribriform plate might, because of its location, likewise escape the hyperostosis.

#### CONCLUSIONS

In conclusion it can be said that hyperostosis frontalis interna is by no means the medical curiosity which the percentages here given appear to make it. There is a total of 65 cases described in the literature, all but 3 being either autopsy reports or composed of museum specimens. To this number 72 living examples of the condition have been added. In spite of the different degrees or types of the disorder the cases have an astonishing similarity to each other and there is variation only in the intensity of the symptoms. Against the severity of the syndrome, one may say tragedy in its full development stands the fact that there are many rational therapeutic measures which may alleviate or possibly arrest the disorder. It is a fact that the picture of the syndrome in its complete form has been published by several writers, description of its less advanced development is something that is new. Two hypotheses regarding hyperostosis frontalis interna have been offered first, that there is a special mechanism for the control of calcium metabolism, existing only in the female, and second, that the disorder of such a mechanism is the cause of the syndrome accompanying hyperostosis frontalis interna. There is presented a field which should be a fruitful one for investigation of those fundamentals which underlie the physiology and chemistry of calcium and fat metabolism, and possibly a hitherto unknown structure with an internal secretion. The disease will be found with far greater frequency if it be sought for. It is possible that investigation of this disorder may throw much light on neuropsychiatric pathology. There is a question as to whether or not the unknown causative factor which

produces the syndrome does not also give rise to the neuropsychiatric symptoms as well as the hyperostosis. Hyperostosis frontalis interna as a name for this syndrome suffers from the drawback inherent in using a single feature of a disorder to designate the whole. It is possible that the hyperostosis, though the surest sign is the least important manifestation of the disease.

## BIBLIOGRAPHY

- CASATI, A. Die senilen Schädelerkrankungen im Röntgenbild. Fortschr. d. Geb. d. Röntgenstrahlen. 926, 34, 335-343.  
 GREGG, D. M. On intracranial osteophytes. Edinburgh M. J. 924, 35, 69-9, 157-260.

- 3 MOREL, FERDINAND. L'hyperostose frontale interne. Syndrome de l'hyperostose frontale interne et adipose et troubles cérébraux. Paris: Gaston Doussard et Cie. 930.
- 4 NASTO, I. Die Hyperostosen des Schädels. Wien: Josef Balz. 924.
- 5 SCHIFF, P., and TAILLER, J. O. Syndrome de Stewart Morel (Hyperostose frontale interne avec adipose et troubles mentaux) d'origine traumatique. Encéphale, 932, 86, 768-779.
- 6 SCHULLER, ARTHUR. Roentgen Diagnosis of Diseases of the Head. Authorized translation by Fred F. Stoenig. St. Louis: C. V. Mosby. 928.
- 7 STEWART, R. M. Localized cranial hyperostosis in the woman. J. Neurol. & Psychopath. 927-28, 3, 3-13.
- 8 V. BODART LUDO. Le syndrome de l'hyperostose frontale interne chez une malade présentant par ailleurs une cécité psychique par béméranopie double. J. Neurol. et de Psychiat. 930, 30, 302.

## A LYMPHATIC CONNECTION BETWEEN THE GALL BLADDER AND LIVER<sup>1</sup>

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FOR many years since the investigations of Sappey (1885) and Sudler (1901) it has been rather generally accepted that a lymphatic connection between the gall bladder and liver exists. Sudler, using for the most part dogs and pigs, injected carmine gelatin into the portal vein at a pressure of 80 millimeters of mercury for 15 minutes and states that by this means he could inject the lymphatics of the liver and in turn the larger lymphatics over the gall bladder and finally those in the subserous coat of the gall bladder.

In 1918, one of us (E. A. G.) described constant inflammatory changes occurring in the liver associated with cholecystitis. These consisted of polymorphonuclear or round cell infiltrations, according to the acuteness of the infection, in the interlobular, or perportal, sheaths. In the more acute infections the parenchyma at the peripheries of the lobules showed infiltration with an associated edema, slight necrosis, and fat infiltration.

Based largely upon the early work of Sudler which demonstrated existence of a lymphatic connection between the liver and gall bladder, one of us (E. A. G.) and co-workers (Priest and Peterman) in 1921, stressed for the first time the probable great importance of the lymphatics as one of the possible routes of infection between the gall bladder and liver regardless of which organ might be primarily affected in a given case. Previous to this time the pathogenesis of infections of the gall bladder and bile tracts was based on four assumed possibilities: (1) descending infection from the liver by bacteria carried down in the bile; (2) ascending infections from the duodenum up the lumen of the common bile duct; (3) hematogenous infections of the gall bladder and ducts; and (4) a spreading infection through the wall of the gall bladder from an inflamed contiguous organ.

That the lymphatic route is an important one has been accepted by many writers.

However, in 1927, Winkenwerder working at Johns Hopkins on the lymphatics of the gall bladder of the cat was unable to demonstrate a connection between the liver and gall bladder. By the direct injection of India ink into visible lymphatics of the subserous plexus of the gall bladder, followed by formalin fixation of the specimen, clearing by the Spalteholz method, and subsequent study of the gall bladder wall under the dissecting binocular microscope, Winkenwerder demonstrated nicely the three lymphatic plexuses in the wall of the cat's gall bladder and the anastomoses of each with the others. However, he states that a careful search failed to reveal any intercommunication between the lymphatic plexuses of the gall bladder with the lymphatic vessels of the adjacent liver tissue.

These observations naturally gave rise to serious doubt as to the actual existence of such a lymphatic connection and in turn challenged the validity of any theory holding the lymphatics responsible in certain cases for hepatitis secondary to a cholecystitis, and vice versa. Hence, it seemed to us important to reopen the question.

### METHOD

The cat was chosen as the experimental animal because of its rather uniform size, the ease with which it is obtained, and, lastly, because it was the only species of animal which Winkenwerder used.

Of the several possible modes of attacking the problem, the one which seemed to us to give promise of offering the most conclusive results was that of direct injection of a dye into visible lymphatics of the gall-bladder wall in the hope that the injected material would appear in the lymphatic spaces of the adjacent liver tissue.

It is a well established fact that in order to obtain satisfactory retrograde injections of the gall-bladder lymphatics, the valves present in

<sup>1</sup>Submitted for publication October 18, 1934.



Fig. Hematoxylin and eosin preparation. The light blue material is the dye, which is injected into the lymphatics of the gall bladder and it is seen here very clearly to be present in perportal lymphatic vessels in the liver. The bile duct, the artery and the interlobular vein

are clearly distinguishable. The only possible source of transport of the dye into the liver under the conditions of the experiment, is therefore subcutaneous lymph channels between the two organs.

some of the larger ones must first be rendered incompetent. This, therefore, was accomplished by utilizing the method described by Lee which consists of ligating under intrathoracic anesthesia the thoracic duct in the chest as a preliminary step, the result being a generalized dilatation of the abdominal lymphatics which causes the valves whenever present to become incompetent. It might be added that unless the animal is fed cream 3 to 4 hours before operation the greatest difficulty is encountered in visualizing the duct.

After waiting 3 to 4 days the abdomen was opened through an upper right rectus incision and the expected dilatation was found. The subserous lymphatics of the gall-bladder wall were usually clearly seen and it was interesting to note that additional dilatation of these can be obtained for a short time by placing a clamp across the cystic duct and adjacent tissues, thus completely blocking the several main lymphatic trunks of the gall bladder.

Benzol's Prussian blue was the dye selected as the injection material and a No. 28 gauge

hypodermic needle and small syringe were used. The needle was carefully introduced into the largest available subserous lymphatic and usually about 1 cubic centimeter of the dye was injected over a period of from one half to one minute. This gave a very clear picture of the lymphatic network of the region injected. Immediately either the entire liver or as was more often the case, the gall bladder and adjacent liver tissue was removed and placed in 10 per cent formalin for fixing, after which routine paraffin sections were made for microscopic study. In some cases sections were taken to show both gall bladder and liver; in others only the liver tissue was included. Two adjacent sections were always stained, one with eosin only so that any of the blue dye present might be readily located, the other with hematoxylin and eosin, that the various structures in the section might be identified in relation to the dye injected.

#### CONCLUSIONS

The dye injected into visible lymphatics in the subserous layer of the gall-bladder wall

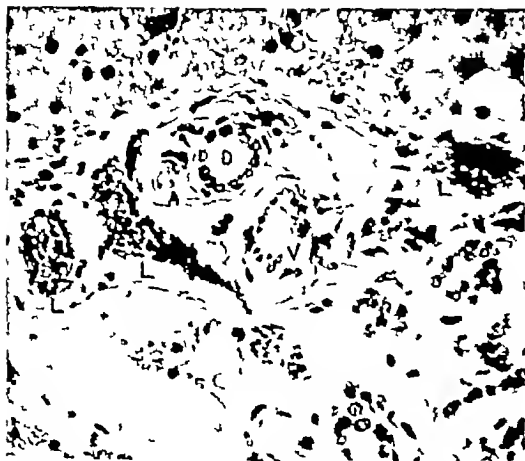


Fig 2 A periportal area containing in a group *L* three lymphatic vessels filled with the injected dye, *I* an artery, *V* a vein, and *D* a bile duct



Fig 3 This shows *I* a longitudinally cut blood vessel and *L* two perivascular lymphatic vessels containing the injected dye. These structures are surrounded by liver parenchyma

was found repeatedly to have passed into the adjacent liver tissue and there to be located in perivascular and periductal endothelial lined vessels in the portal spaces. As will be noted in the illustrations the usual picture shows an epithelium lined bile duct, an artery and vein containing red blood cells, and one or more endothelium lined vessels with the dye present in a group and surrounded by liver cells.

This evidence seems therefore definitely to substantiate the earlier work of Sudler in demonstrating the existence of an intimate lymphatic anastomosis between the gall bladder and the liver. These particular experiments of ours have shown the transportation of the dye only into the portion of liver immediately adjacent to the gall bladder. But from what is already known about the distribution of the lymph in the liver from the work of Mall, there is good reason to suppose that the dye in time would have been found elsewhere at least in other parts of the right lobe, if the experimental method had permitted finding it. Since, however, only very small amounts of dye were used, it was difficult to recognize its presence at more remote parts of the liver where it would occur in only very slight concentration. At any rate the anatomical evidence of the hepatitis which occurs in association with cholecystitis is most marked in the

right lobe of the liver and particularly in that part of it which is immediately adjacent to the gall bladder. In other words the agreement between the distribution of the dye transported to the liver by way of the lymphatics and the distribution of the histological evidences of inflammation seem to lend additional support to the idea that at least in some cases there is a lymphatic transport of infection between gall bladder and liver.

The fact that, as Noble has recently emphasized at postmortem examination there is frequently found an infiltration of the periportal spaces with lymphocytes and polymorphonuclear leucocytes regardless of any demonstrable disease of the gall bladder has little to do with the point under discussion in this paper. We have never proposed that the gall bladder is the only source of a periportal lymphangitis in the liver.

#### BIBLIOGRAPHY

- 1 GRAHAM, E. A. *Surg., Gynec. & Obst.*, 1918, 26 521
- 2 GRAHAM, E. A. and PETERMAN, M. G. *Arch. Surg.*, 1922 4 23
- 3 LEE, F. C. *Bull. Johns Hopkins Hosp.*, 1922, 33 21
- 4 MALL, F. P. *Bull. Johns Hopkins Hosp.*, 1901, 12 146
- 5 NOBLE, J. F. *Am. J. Path.*, 1933, 9 473
- 6 PETERMAN, M. G., PRIEST, W. S., and GRAHAM, E. A. *Arch. Surg.* 1921 2 92
- 7 SUDLER, M. T. *Bull. Johns Hopkins Hosp.*, 1901, 12 26
- 8 WINKENWERDER, W. L. *Bull. Johns Hopkins Hosp.*, 1927 41 226



# CLINICAL SURGERY

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## RECONSTRUCTION OF THE FEMALE URETHRA

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### OPERATIVE TECHNIQUE

FIVE patients afflicted with complete destruction of the urethra in association with vesicovaginal fistula have been encountered by the author in the past 10 years. Twice the lesion was due to sloughing following childbirth, and on the other 3 occasions was the outcome of the surgical treatment of carcinoma of the urethra by resection diathermy or radium used either alone or in various combinations.

Since in the circumstances for which the operation is to be undertaken, the bladder sphincter and posterior wall of the urethra have been more or less completely destroyed for this reason it will be necessary not only to fashion a new urethra but also to provide it with an efficient cut-off muscle.

As no recorded type of operation for this comparatively rare lesion appears to have inspired any kind of enthusiasm, or to have been hailed with even the mildest degree of satisfaction, and especially as reports still continue to appear in the literature of results, too often only partially successful, which have followed attempts at the surgical repair of this condition (cf. McGlenn and George Gray Ward) the author has been prompted to place on record again an operation which he has employed with success in the treatment of the 5 patients here mentioned. The results obtained, from the patients point of view appear to leave little room for improvement. All have complete bladder control.

In the case of the first three of these patients a brief description of the operation was presented at the first annual meeting of the Royal Australasian College of Surgeons held at Canberra in March, 1928, and was published in *The Journal of the College of Surgeons of Australasia* (March, 1929). Since that publication some small technical modifications have been made. The operation has now been redrawn and is described herewith in further detail.

Some tags or bands of tissue are liable to be present in the region of the urethra, especially in post-obstetric cases. These should be trimmed off level with the vaginal mucosa and allowed to heal before the plastic operation is undertaken.

Briefly the operation consists of making a U-shaped incision surrounding the vesicovaginal orifice the open end of the U terminating at the original site of the external orifice of the urethra (Fig. 1). The incision is deepened for about 3 millimeters (one-eighth of an inch) and the vaginal wall beyond the line of incision is undermined all round to form lateral flaps. The portion of the vagina embraced by the U-shaped incision is not further disturbed, except by the sutures employed to bring its edges together in the midline to reform the urethral tube (Fig. 1, inserts a, b and c). A new sphincter is then fashioned from the muscles of the bladder base as will be described below (Fig. 2 insert a) and the lateral flaps are sewed together over-all, the restoration of the urethra being thus completed (Fig. insert b). Actually the neighborhood of the fistula is covered by three or four superimposed layers, whereas in the lower part of the new urethra only two layers are formed. A suprapubic cystostomy concludes the operation. Urethral drainage is not practiced.

The operation is very simple and makes use of principles well known in the plastic surgery of the male urethra. The absence of tension leaves little room for failure when reasonable precautions are taken.

It will perhaps, not be amiss if some features of the operative technique be described in further detail.

After the U-shaped incision has been outlined, the lateral dissection must be carried fairly deeply and widely in the region of the base so as to allow a good exposure of the bladder muscle in the

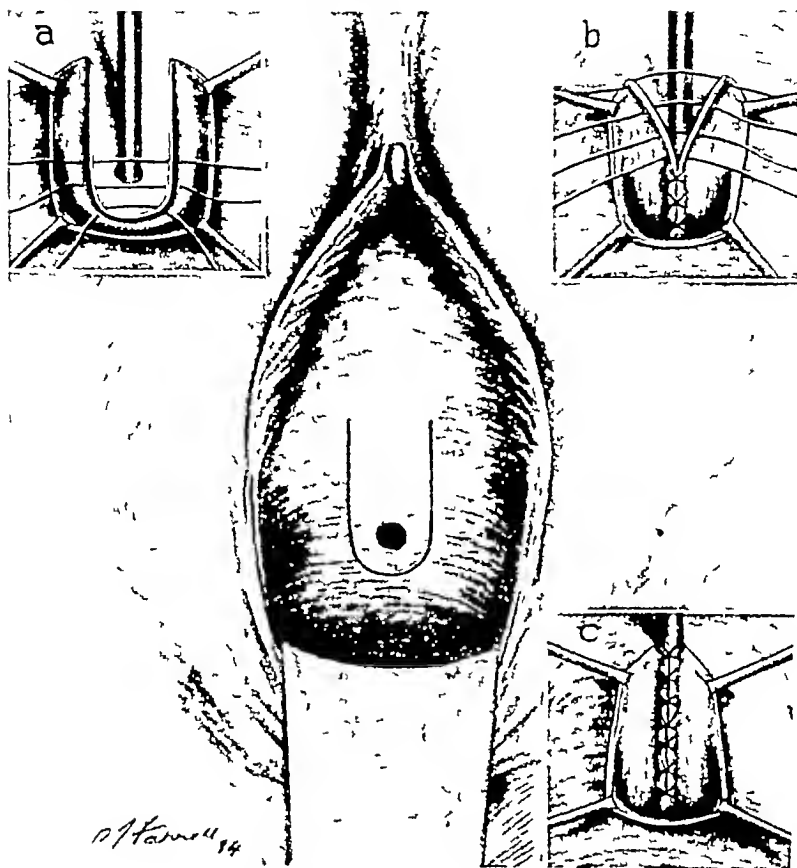


Fig 1 Showing U shaped incision around orifice of vesicovaginal fistula and site of urethra a, Showing Young's seminal vesicle tractor in the bladder and first three sutures in position, but not tied In practice each suture is tied as it is inserted b First three urethral sutures tied, the remainder inserted but not tied c, All urethral sutures tied, urethral tube reformed

neighborhood of the fistula Toward the free ends of the U, however, there is no underlying bladder muscle and the dissection in this situation should be much more superficial (Fig 2) If the dissection be carried too deeply, large venous plexuses may be encountered, the bleeding from which may be difficult to control This mistake was actually made in the first 3 cases in an endeavor to obtain more tissue than was absolutely necessary In the last 2 patients, care was taken to dissect only deeply enough in this situation to allow easy approximation of the cut edges

Young's seminal vesicle tractor was employed in the last 2 cases and is a great improvement on the de Pezzer catheter which was employed in the first three An instrument of this type is invaluable in delineating the bladder neck and so in

indicating the exact situation for the insertion of the sutures for the sphincter reformation

In the process of reforming the sphincter, if a sufficiently firm grip of the tractor is not afforded, when the two sutures illustrated have been tied, another suture should be placed more widely at a level midway between these two sutures This additional sphincter suture was employed in each of the last 2 cases, and could probably be employed with advantage in all The tractor is kept in position until the completion of the plastic operation

Chromicized gut No 0 is used for the first or innermost layer of sutures, No 3 plain catgut for the sphincter sutures, and silk-worm-gut for the final vaginal sutures As large a bite of the tissues as is reasonably possible is included in each suture

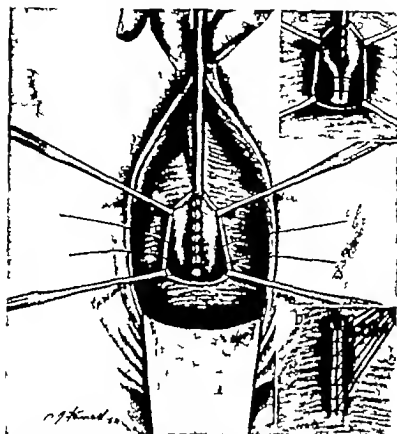


Fig. Showing the two sutures in position for reformation of the sphincter. a, Sphincter sutures tied. b, Completed operation individual sutures uniting the vaginal sinuses in the midline.

Interrupted sutures of silk worm-gut for the outer layer were used only in the last two patients and *per primam* union resulted. Equally good results were previously obtained when continuous catgut sutures were employed, but it is believed that in a larger number of cases, slightly higher degree of certainty would be obtainable with the interrupted silk worm-gut sutures. These may be left in position until the twelfth or fourteenth day when the suprapubic drainage is dispensed with. Rapid closure of the suprapubic wound ensued in all cases.

#### CONCLUSIONS

A perusal of the literature would lead one to believe that the necessity for an operation of the

type described arises more commonly in America than in England or Australia. Recorded cases are, however, by no means always an accurate guide to local conditions. Be this as it may the author's operation is presented to his American colleagues in the fervent hope that, should the occasion arise the operation will yield results in their hands at least as satisfactory as it has in his.

#### REFERENCES

- McGILVER, JOHN A. Reconstruction of the urethra. *Am. J. Obst. & Gynec.*, 93, 34, 36.  
 W. ED. GARDNER GRA. Destruction of the urethra and loss of vesical control associated with carcinoma of the vulva. *Surg. Gynec. & Obst.*, 93, 57, 67.

## PULMONARY EMBOLISM FOLLOWING TRAUMA

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NUMEROUS papers have been written on traumatic thrombosis without embolism but, of the almost countless papers on pulmonary embolism only a few are devoted to the type following injury. These are mostly isolated case reports. The only large reviews I have found are those of Bruns (1886), Lotheissen (1902), and Daus (1913).

In 1927, I reported 23 cases of pulmonary embolism following injury and found 119 cases in the literature. Since that time a considerable number of instances of post-traumatic embolism have been reported, many only as incidental to the whole problem of embolism of the lung and not in sufficient detail to permit of tabulation. Lister (1927) reported 12 cases following fractures in a series of 281 pulmonary embolisms. Of the 12, 9 followed fracture of the femur, an incidence of 11 per cent in 80 fractured femurs. Henderson (1927) reported 5 cases in a series of 313 embolisms, 3 of them following reduction of fractures of long bones. Hoering (1928) reviewed 3,248 autopsies, finding 131 instances of pulmonary embolism, 10 of which were post-traumatic. Of the 10 cases, 4 followed fracture of the femur. Martini (1928) reported 90 cases of pulmonary embolism from a series of 3,193 autopsies. Five of the embolisms followed fracture. In a series of 113 cases of embolism reported by Miller and Rogers (1929), 7 followed fractures but necropsies were done in only 4 of these traumatic deaths. Killian (1930) reported 102 instances of embolism, tabulating 35 of these. In his table 5 instances of postfracture embolism are cited. Orator and Straaten (1930) found 3 of post-traumatic origin among 17 fatal embolisms. Sarafoff (1930) mentioned 19 instances of embolism after fractures in reporting 95 fatal embolisms, 88 of which were verified by autopsy.

A review of the necropsy records in the Department of Pathology of the University of Minnesota for the period January 1, 1927, to July 1, 1933, revealed 9,781 cases which are suitable for analysis from the standpoint of pulmonary embolism. The postmortem records of stillbirths, newborns in whom no adequate cause of death was found, and partial examinations were rejected. Analysis shows that for the purposes of this paper 1,499 (15.3 per cent) were deaths from mechanical injury. Of the 1,499, 1,174 were males and 325

females, a ratio of 3.6 to 1. In the entire series of necropsy records examined the ratio of males to females is 1.7 to 1. For the entire series the incidence of pulmonary embolism is 2.8 per cent.

In the traumatic group, there were 61 pulmonary embolisms, an incidence of 4.0 per cent. In the non-traumatic group there were 222 embolisms, an incidence of 2.6 per cent. Statistically this appears to be a significant difference. Of 283 deaths due to pulmonary embolism, 61, or 21.6 per cent, followed trauma. In other words, 15.3 per cent of the cases analyzed accounted for 21.6 per cent of the fatal pulmonary embolisms.

The age distribution of the cases is about the same in the two groups. For the entire series studied the incidence of pulmonary embolism is 2.5 per cent in males and 3.6 per cent in females. This appears to be a significant difference. The greater incidence in females is not to be accounted for by the embolisms which followed childbirth (11 cases). The incidence of embolism after trauma is 2.8 per cent in the male and 8.6 per cent in the female. This difference is significant.

Four possibilities suggest themselves as explanations of this sex difference in the incidence of post-traumatic pulmonary embolism: (1) The age distribution of the cases may be different in the two sexes. (2) Heart disease may be more frequent in females than in males. (3) Perhaps more of the males died shortly after being injured, because of the greater liability to industrial accidents. (4) There may be anatomical differences in the blood vessels of the pelvis and lower extremities in the two sexes.

An analysis of these cases was made in an attempt to find answers to these possibilities. Table I shows the age distribution of the traumatic deaths by sex, by number, and percentage of cases and incidence of pulmonary embolism. From this table it appears that there was, on the whole, no very great difference in the age distribution in the two sexes, the first, fifth, and eighth decades showing the greatest discrepancies. On the other hand, the sex difference in the incidence of pulmonary embolism is very striking. It would appear that, in this series of cases, the difference in incidence of pulmonary embolism in the two sexes is not to be explained on the basis of age.

The series was then examined for the incidence of anatomical heart disease. It was found that

<sup>1</sup>Acknowledgment is hereby made of assistance received from the Civil Works Administration.

TABLE I.—AGE AND SEX DISTRIBUTION OF TRAUMATIC DEATHS AND PULMONARY EMBOLISMS

Age	Males				Females			
	No. cases	Per cent	No. deaths	Incidence embolism per cent	No. cases	Per cent	No. deaths	Incidence embolism per cent
1-10	31	6			26			
11-20	39				13			
21-30	20				29	6		
31-40	137	10.8			46	1		
41-50	64	14			31	8		8
51-60	26	2			26	11.6	8	8
61-70	18			6	40	1	6	15
71-80	113	10	8	6	30		6	
81-90	42	6			2			
91-100	28							
Adult	17				61	6		
Total	77		12	6	275		26	8.6

heart disease was present in 20.5 per cent of the males and 18.4 per cent of the females. This obviously does not account for the sex difference in occurrence of pulmonary embolism.

Since no patient died of pulmonary embolism within the first 24 hours after being injured (Table V) the series was examined after eliminating the deaths occurring during this period of time. This procedure left a total of 722 cases—553 males and 170 females—to be studied. The incidence of pulmonary embolism was then 5.9 per cent in males and 16.4 per cent in females. These 722 cases were then studied from the standpoint of the presence or absence of anatomical heart disease and the occurrence of embolism. This study revealed that the incidence of embolism was, in the non-cardiac group 5.5 per cent in males and 13.6 per cent in females, and in the cardiac group 7.1 per cent in males and 24.9 per cent in females. No help in explaining the sex difference in incidence of pulmonary embolism was obtained by these analyses.

This series of cases did not lend itself to analysis from the standpoint of attempting to answer the fourth of the above listed possibilities. So far as I can learn there are no normal anatomical differences in the blood vessels of the pelves or lower extremities which might account for the sex difference in incidence of post-traumatic pulmonary embolism. However it is well known that varicose veins are much more frequent in females than in males after the age of 30 years.

TABLE II.—AGE DISTRIBUTION OF DEATHS AND PULMONARY EMBOLISMS

Age	Traumatic			Non-traumatic			Total per cent of embolism
	No. of deaths	No. of embolisms	Per cent of embolisms	No. of deaths	No. of embolisms	Per cent of embolisms	
1-10	167			26			
11-20	39			137		6	
21-30	20			61			6
31-40	137			46	26	6	6
41-50	64			31	22		1
51-60	26	7.6	13.6	40	3		
61-70	18	7	14.3	44			6
71-80	113	6	8.1	27			7
81-90	42			2			6.6
91-100	28			2	6		6.6
Adult	17			133		6	8
Total	1,200	62	8.6	275	26	6	8

McPhetters (1931) gives the ratio of varicose veins as 4 in the female to 2 in the male. Unfortunately the present series gives no clue as to the frequency of varicose veins, but it is reasonable to assume that diseased vessels would be more susceptible to trauma than normal ones. It may well be that the real explanation for the higher incidence of post-traumatic pulmonary embolism in females is this greater frequency of varicose veins.

The distribution of deaths and embolisms by decades and the incidence of embolisms in the various decades is shown in Table II. It is apparent that in both groups, the maximum incidence of pulmonary embolism is between the ages of 50 and 80 years, although it may occur at any age. The wider age distribution of embolisms in the non-traumatic cases is apparent.

Table III shows the same findings somewhat more clearly by percentages. In persons of known age in the traumatic group 5 per cent of the cases occurred in this age period, whereas in the non-traumatic but 57.1 per cent were in the same period. The great importance of age in the causation and occurrence of embolism is very clearly brought out in these tables. It is probably not merely the age that is of importance but rather

supposition of this table with age given in 10 years groups is apparent at all in the decade distribution of cases shown. The present findings are more nearly in agreement with those of other series in that the earlier table (I) appears that sex occurred. This suggests that sex and an important factor in causation is apparently important factor in the occurrence of embolism. A possible explanation for the discrepancy in the two tables may be in the increased care used in the search for emboli in the more recent inquiries.

TABLE III—AGE DISTRIBUTION OF PULMONARY EMBOLISM BY PERCENTAGES OF EMBOLISMS

Decade	Traumatic	Non traumatic	All cases
1		0 9	0 7
2	1 6	0 9	1 0
3		5 8	4 5
4	6 5	11 7	10 6
5	9 8	14 8	13 7
6	24 5	20 2	21 2
7	27 8	19 8	21 5
8	22 9	16 6	18 0
9	4 9	7 6	7 0
10		0 4	0 3
Adult	1 6	0 9	1 0

the accompaniments of age, viz, the decreased muscular activity with resulting impaired tone of the muscles, the high incidence of cardiac disease, the tendency to obesity, the greater incidence of debilitating disease, etc., all of which tend to slow up the circulation

Inasmuch as there are almost no large series of cases of post-traumatic pulmonary embolism recorded, I believe that as detailed a description of such a series as space will permit may be of value. It is realized that many defects exist in individual cases of this series and that if the data were available their usefulness would be greatly increased

## CASE REPORTS

CASE 1 (31-24.) A fairly well nourished female, aged 52 years, had sustained an intracapsular fracture of the right femur, 35 days before death. Four or five days before death she had a sudden attack of dyspnea, cyanosis, and pain in the chest. There was bloody sputum on coughing. She recovered from this attack. Death took place suddenly. Autopsy findings embolus in main pulmonary artery, infarct in left lung, thrombosed right common iliac vein, heart normal (257 grams)

The symptoms appearing 4 or 5 days before death should have made one suspect embolism. This was probably the time when the infarct in the right lung developed

CASE 2 (32-2038) Patient was a poorly nourished female, aged 52 years. She had fallen 25 days before death and had fractured the neck of the left femur. She was treated by traction and Jones splint. She got along well until the day before death when the temperature was found to be 100.0. The day of death the temperature was 104 degrees. The manner of death was not described. Autopsy findings embolus in artery of right lower lobe, thrombosed left femoral, external iliac and aphenous veins, edema of the left knee, bronchopneumonia, heart normal (100 grams)

CASE 3 (32-1664.) A fairly well nourished male, aged 52 years had fallen down stairs 8 days before death, sus-

TABLE IV—TYPES OF INJURY WITH NUMBER OF CASES AND INCIDENCE OF PULMONARY EMBOLISM

	No	I P	Per cent I P
Fractures	415	1	0.2
Skull	109	2	1.8
Ribs	68	1	1.4
Spine	25	2	8.0
Arm	31	1	3.2
Pelvis	29	8	27.5
Tibia and/or fibula	118	27	22.9
Femur	251	13	5.2
Multiple bones	134		
Gunshot	289	6	2.1
Miscellaneous trauma	1,491	1	0.1
Total			

taining an impacted intracapsular fracture of the left femur. His course was satisfactory, the temperature was 100.0, 24 hours above 99.2 degrees, the leucocyte count was 15,000. 24 hours before death he had an attack of right lower lobe pneumonia and an epileptiform seizure. There was bloody sputum on coughing. Autopsy findings embolus in main pulmonary artery, free thrombus in vena cava, thrombosed right femoral fracture and right common iliac vein, infarct in right leg, heart normal (355 grams)

It is to be noted that in this case there are two possible sources for the embolus, the region of the fracture and the right lower lobe. One may be an extension of the embolus from the right side, although some would doubt this

CASE 4 (29-674) Patient was a female, aged 49 years. She had collided with a car, fracturing the neck of the left femur. Some hours before death she had a sudden attack of dyspnea and appeared to be in shock. Autopsy findings embolus in both lungs, antemortem thrombosis of right lower extremity, heart normal (257 grams)

CASE 5 (30-946) Patient was a female, aged 58 years. She had fallen 24 days before death, fracturing the neck of the left femur. About 1 week before death she developed a painful phlegm in the right thigh. On the 23rd day of illness, twenty third days before death, she died. There were slight rigors 24 hours before death. Third day several days before death severe dyspnea. Autopsy findings embolus in main pulmonary artery, infarct in left lung, thrombosis of right femoral and greater saphenous veins, right extremity normal, heart normal (257 grams)

This is an excellent example of the source of the embolus, the trauma of the fracture formation 24 days before death, dyspnea, the infarcting of the right lung, embolism

CASE 6 (30-946) Patient was a female, aged 61 years, 24 days before death, fracturing the neck of the left femur. About 1 week before death she developed a painful phlegm in the right thigh. On the 23rd day of illness, twenty third days before death, she died. There were slight rigors 24 hours before death. Third day several days before death severe dyspnea. Autopsy findings embolus in main pulmonary artery, infarct in left lung, thrombosis of right femoral and greater saphenous veins, right extremity normal, heart normal (257 grams)

TABLE V—TIME OF PULMONARY EMBOLISM  
AFTER TRAUMA  
6 Cases

Interval	Cases	Total
4 days	1	1
5 days	1	1
6 days	1	1
7 days	1	1
Second week	1	1
Third week	1	1
Fourth week	1	1
Later	1	1
Total cases	6	6

location and fracture of the head of the right femur. Several attempts were made to reduce the fracture. On the day of death, under spinal anesthesia, reduction was accomplished and cast was applied. While still on the table, he suddenly became cyanotic (Was the embolism responsible for the loosening of the thrombus?) Autopsy findings: embolus in right pulmonary artery; thrombosed right iliac vein, branching of both thighs, especially the right; heart normal (400 grams).

CASE 7 (3-103) The patient, an obese female, aged 63 years had been in an automobile accident 8 days before death, and had sustained fractures of both femurs and laceration of the forehead. X-ray examination revealed comminuted fracture of head and lower half of right femur. The day before death the right femur was manipulated and Stimson cast was applied. Subsequently she complained of pain in the leg. She grew weaker and her respirations were rapid. She became semicomatose and later comatose. Autopsy findings: bilateral embolus of the pulmonary arteries, infarcts in both lungs, source of emboli undetermined, carotid artery embolus (?), heart normal (568 grams).

This case is included in the group of fractures of the femur rather than in the group of multiple fractures in Table IV. This patient showed none of the usual symptoms of pulmonary embolism.

CASE 8 (3-129) An obese male, aged 63 years, had fallen 13 days before death, and had sustained transverse fracture of the middle third of the right femur. Traction was applied. Six days before death he began to complain of pain in the right thigh. Four days before death, ether was administered for the application of calipers. Course was quite satisfactory. His temperature varied from 98 to 101 degrees. There was sudden attack of dyspnea with marked cyanosis, but no pain. He was dead in minutes. Autopsy findings: embolus 5 by catheter packed from the pericardial sac following removal of the heart, infarct of the right lung, thrombosed right internal iliac vein, heart hypertrophied (475 grams).

The embolism which was responsible for the infarction of the right lung apparently gave no symptoms. The finding of a well developed infarct in the lungs is rather frequent in cases of suddenly fatal embolism, although the earlier non-fatal embolism may not have caused symptoms.

CASE 9 (3-667) The patient who was well over 60 years of age, aged 65 years, about 6 weeks before death had suffered comminuted fracture of the lower third of the right femur involving the knee joint. The knee was excised

3 times, 6 weeks, and 8 days before death, and post mortem was obtained. Temperature was 100 degrees. Leucocytes count was 400 polymorphonuclears per cent. Temperature ranged from normal to 103 degrees. Blood pressure was 16/96. She was stuporous most of the time. Autopsy findings: gas gangrene, right thigh involved, abscess several inches filled with thick creamy pus, gas bacilli septicaemia, multiple small emboli in both lungs, source not found, infarct of right lung, chestnut paste congestion of lungs, heart normal (400 grams).

CASE 10 (30-06) A fairly well nourished female, aged 67 years, had fractured her right femur 5 days before death. Her course was favorable until sudden death. Autopsy findings: bilateral pulmonary embolism; thrombosed right femoral vein and veins in brachial area above fracture; heart, coronary arteries (150 grams); edema of right leg, right thigh larger than left.

CASE 11 (30-165) A fairly well nourished female, aged 48 years, had fractured her left femur 4 weeks before death. The left leg was braced. A cast was applied. The progress was favorable for a time. Later she complained of dizziness and nausea. Subsequently she went into coma. During the last 24 hours, there were diarrhea and cramps. Systolic blood pressure was low. She was diabetic with blood sugar, 83. Autopsy findings: pulmonary embolism, infarcts in both lungs, edema of left leg, brachial area of left leg source of emboli not found, heart showed hypertrophy and coronary arteries (400 grams).

The symptoms together with the hypertension and diabetes mellitus, might well have suggested a cerebral accident or diabetic coma rather than pulmonary embolism.

CASE 12 (30-1255) A well nourished male, aged 69 years, 3 days before death had fractured the neck of the left femur and had bruised the soft tissues. About 24 to 36 hours after the fracture he became delirious and had temperatures of 103 degrees. Autopsy findings: bilateral pulmonary embolism, thrombosed left femoral vein, bronchopneumonia, heart normal (400 grams).

CASE 13 (3-1786) An obese female, aged 69 years, was in an automobile accident 9 days before death, and had suffered an intertrochanteric fracture of the left femur, laceration of the scalp, concussion (?). She was unconscious for short time. Her course was stable and favorable. She died suddenly. Autopsy findings: embolus in main pulmonary artery and the large branches—source not found, heart normal (345 grams).

CASE 14 (3-1254) A poorly nourished male, aged 69 years, fell 3 days before death, producing an intracapsular fracture of the left femur. A cast was applied. Twelve days afterwards he had resty symptoms, later it was bloody. He had sharp pain in the right lower chest with distress and cyanosis. Temperature was normal. Diagnosis: bronchopneumonia. Later temperature rose to 103 degrees. Nine days before death temperature was 3 degrees. The day of death he had chills, but temperature was 104.3 degrees. Autopsy findings: bilateral embolism, embolus partially adherent but folded—source not found, edema of right leg and thigh, heart normal (350 grams).

The symptoms, complained of 1 day before death and diagnosed "bronchopneumonia," may well have been those of embolism with infarction. At necropsy neither bronchopneumonia nor infarction was found.

CASE 15 (32 1544) Patient was a well nourished male, aged 69 years. He fell 14 days before death, fracturing the left femur. Death was sudden. Autopsy findings embolus in main trunk of pulmonary artery, thrombosed left femoral vein in region of fracture, heart normal (350 grams).

CASE 16 (27-652) A poorly nourished female, aged 70 years, fell 12 days before death, fracturing the right femur. Her blood pressure was 134/22. The day of death she was up on crutches. She had an attack of weakness and coldness, collapsed and died in about 3 minutes. Autopsy findings main and bilateral embolism, partially adherent, thrombophlebitis of right leg, edema of right leg, thigh and left ankle, heart normal (271 grams).

CASE 17 (30-43) Patient was an emaciated female, aged 72 years. She fell 18 days before death, sustaining an impacted intracapsular fracture of the neck of the left femur. Taking advantage of the enforced rest, she had a facial tumor removed on the day of death. There was difficulty in breathing at the start of the operation (local anesthesia). She died suddenly the same day. Autopsy findings embolus right pulmonary artery—source not found, chronic passive congestion of lungs, heart normal (310 grams).

CASE 18 (28-1019) The patient, a fairly well nourished male, aged 73 years, fell 93 days before death, suffering a fracture of the neck of the left femur. It was treated by traction. Two days after the fall the leucocyte count was 19,100, 1 month later 27,000. He was up and about 3 days before death, feeling well. While walking he suddenly fell over and died. He had hypertension and the blood pressure was 204/90. Autopsy findings embolus in left pulmonary artery, thrombosed left femoral and hypogastric veins, edema both lower extremities, especially the left, heart, hypertension (350 grams).

CASE 19 (30-1004) Patient was a fairly well nourished male, aged 73 years. He fell 13 days before death, sustaining a comminuted fracture of the left femur extending into the knee joint. Treatment consisted of extension and application of a Thomas splint. The extremity was manipulated 4 days before death, a Steinmann pin was put in 3 days before death under nitrous oxide anesthesia. Two days before death he vomited decomposed blood, had a chill, temperature of 103 degrees, pulse of 140, was cyanotic and stuporous, but had no pain. One day before death abdominal distention developed, temperature normal. One and one half hours antemortem he had chill, weakness, cyanosis, and thready pulse. Axillary temperature was 103.8 degrees. Autopsy findings small bilateral pulmonary emboli, antemortem clot which was milked from veins of left lower extremity, edema of left lower extremity, heart, coronary sclerosis and myocardial fibrosis (425 grams).

CASE 20 (33 296) Patient was a well nourished female, aged 74 years. She fell 25 days before death, suffering a fracture of the left femur. Blood pressure was 148/78. Forty two hours before death she became restless and unresponsive, had twitchings of hands and arms, cyanosis, stertorous respirations, pulse rapid and feeble, incontinent (history of similar attacks in the past). These symptoms continued until death. Temperature was 102 degrees. The day of death she became weaker, respirations shallow and irregular, at times of Cheyne Stokes type. Autopsy findings embolus in main pulmonary artery, thrombus milked from left femoral vein, heart, pericardial space obliterated (375 grams).

The symptoms in this case suggest some cerebral lesion rather than pulmonary embolism. Cerebral symptoms are not rare in pulmonary embolism.

CASE 21 (29 375) A moderately nourished male, aged 74 years, fell 5 days before death, fracturing his right femur through the trochanters. A cast was applied. The blood sugar was high. The night before death the temperature was 100 degrees. Death was rather sudden. Autopsy findings multiple small emboli, thrombus milked from veins of right lower extremity, heart normal.

CASE 22 (25 27) A well nourished male, aged 75 years. He fell 15 days before death and sustained a comminuted fracture of the left hip and a simple fracture of the lower third of the left femur. A cast was applied. Thirty six hours antemortem cyanosis, marked respiratory difficulty, and congestion of the lungs developed. He improved after a few hours. Sudden death occurred the next evening. Autopsy findings emboli in both lower lobes, embolus in ventr. cava from diaphragm to tricuspid valve, thrombosed left femoral vein, heart, calcified aortic valve defect (425 grams).

CASE 23 (31 414) A fairly well nourished female, aged 75 years, fell out of bed 9 days before death, suffering a comminuted intertrochanteric fracture of the right femur. Temperature varied from 99 to 102 degrees. Two days antemortem she became unconscious. Blood pressure was 150/80. Autopsy findings embolus in right pulmonary artery, thrombosed left common iliac vein and vena cava, encephalomalacia with hemorrhage, abrasions of right knee and thigh, bronchopneumonia, heart normal (347 grams).

Perhaps objection might be made to this case as an embolic death, since cerebral softening and hemorrhage were present. These intracranial lesions undoubtedly caused the unconsciousness. The manner of death was not described. There was pulmonary embolism, whether or not it caused death.

CASE 24 (32 142) A poorly nourished female, aged 77 years, fell 83 days before death, sustaining an intertrochanteric fracture of the right femur. A cast and Jones splint were applied. She gradually grew weaker. Several days before death the respirations became labored. Autopsy findings embolus left pulmonary artery, thrombosed right and left femoral veins, secondary acute tricuspid bacterial endocarditis (290 grams).

In this case there were three possible sources for the embolus in the lung. Which one was the source was not determined. The presence of tricuspid endocarditis suggests that in this case infection may have played a part in the development of the bilateral femoral vein thrombosis.

CASE 25 (32 682) A poorly nourished female, aged 80 years, fell 17 days before death, and suffered a fracture of the right femur. Hypertension was noted with blood pressures 170/83, 206/78, 260/140. She had had edema, dyspnea, palpitation, and weakness for 1½ years. Two weeks antemortem she showed edema and marked dyspnea. There was progressive weakness. The temperature was normal except for a terminal rise. Autopsy findings bilateral small emboli, infarct right lung—source not found, bronchopneumonia, heart, hypertension (380 grams).

It is indeterminate in this case whether the symptoms were due to hypertension or embolism. The infarct apparently gave no sign of its presence.



CASE 26. (24-83) A fairly well nourished female aged 85 years, fractured the neck of the left femur 3 days before death. Hypertension was noted. 11th blood pressure 15/100. Abatement of breath edema. She gradually grew weaker and apparently died of heart failure. Autopsy findings: small emboli in left large—source not found. Edema, especially of left leg. Chronic passive congestion of liver heart, hypertrophied (350 grams).

It may be argued that this death should be charged to the decompensated heart disease and not to the pulmonary embolism and that the embolism is a complication of decompensation and is of the nonfatal form.

CASE 27. (27-26) A poorly nourished female aged 80 years, had fallen 3 weeks before death, sustaining dislocation of the left femur. She became short of breath 4 days before death, cough 3 days with fever and bloody sputum. Edema of ankles week before death enlarged to left systolic murmur at apex. Blood pressure 40/90. Autopsy findings: embolus right lower lobe—source not found in femur right long. Edema of ankles, chronic passive congestion of liver heart, mitral and aortic valve defects, myocardial fibrosis (408 grams).

In Table IV this case is included with the fractures of the femur because the local trauma and the type of treatment would undoubtedly be about the same as in fracture. Here again the part played by the heart disease and the embolism is indeterminate.

Seven other cases with fractured femurs might well have terminated with pulmonary embolism. A source for an embolus was found in each but detachment of the thrombus did not take place.

CASE 28. (3-87) A fairly well nourished male, aged 75 years, fractured his right tibia and fibula 20 days before death. Cellulitis of the left arm developed following burn suffered one or more days before death. Blood pressure was 90/60. He had labored respiration with shallow breaths. Autopsy findings: multiple small emboli source not determined. Edema of left arm heart, mitral ab- defect with acute rheumatic mitral endocarditis (200 grams).

The question may be raised whether the burn sustained played an part in the development of an undiscovered thrombosis and the resulting embolism.

CASE 29. (10-64) A fairly well nourished male aged 69 years, had a comminuted fracture of left tibia and fibula, sustained 20 days before death. It was plastered 3 days before death. Fever had this abatement. Local thrombophlebitis, osteomyelitis, and carcinoma of the prostate. Hypertension was noted with blood pressure 75/90. Temperature was 99 degrees and cyanosis, weak rapid pulse and distress were present. Autopsy findings: bilateral embolism, cardiac porphyria, thrombosed left coronary sinus and branches and left internal iliac veins. Left atrial planes congestive heart hypertrophy myocardial fibrosis (350 grams).

This case is rather complicated because of the large number of pathological lesions present and

it is very difficult to determine what etiological role each played in the development of the thrombosis and embolism. The part played by the trauma, the operation, the infection, the cardiac and the malignant disease in causing death are indeterminate.

CASE 30. (30-99) A well nourished male aged 24 years, sustained a comminuted fracture of the left tibia and fibula 30 days before death. Seven to ten days before death he had bloody sputum. Death was rather sudden. Autopsy findings: embolus in main pulmonary artery and its large branches, infarcts in both lungs, thrombosed right external iliac and femoral veins and deep vein left lower extremity heart, hypertrophied (?) (475 grams).

It is probable that the initial pulmonary embolism with infarction took place 7 to 10 days before death. The bloody sputum should have served as a warning of the possibility of a fatal embolism. Here again there are two possible sources for the emboli, one near the site of the fracture and the other in the opposite extremity. Whether there was also injury of the right lower extremity is unknown.

CASE 31. (3-108) A well nourished male aged 41 years, fractured his right tibia and fibula 4 days before death. A Mennen's poultice was inverted 25 days before death, and cast was applied. Early in his illness he felt well and wanted to get up 5 days previous to death but became very cyanotic, short of breath, and complained of his heart. Autopsy findings: embolus in main pulmonary artery, bilateral infarcts, thrombosed right femoral, right iliac, popliteal veins. Fracture and cast on right lower extremity discolored and swollen, heart hypertrophied (?) (250 grams).

CASE 32. (27-5) An obese female, aged 53 years, fractured her right tibia 3 weeks before death. X-ray examination showed comminution of lateral condyle of the tibia. Suppurative prepatellar bursitis developed. Cast was applied. Death was sudden. Autopsy findings: embolus in main pulmonary artery, thrombosed right popliteal vein heart normal (300 grams).

CASE 33. (33-45) A poorly nourished male aged 61 years, fractured both tibia and fibula in an automobile accident 6 days before death. Autopsy findings: small embolus of lower lobe of right lung, thrombosed right carotid and iliac veins cerebral hemorrhage and meningeal hemorrhage, heart normal (300 grams).

This case was grouped with the fractures of tibia and fibula in Table IV instead of with the multiple fractures, because the fractures were of the same bones even though bilateral. The question may be raised whether death should not be attributed to the brain injury rather than to the embolism.

CASE 34. (40-13) A well nourished male, aged 53 years, 11 months before death, fracturing the lower end of the right fibula and the left os calcis. A cast was applied. Autopsy findings: multiple small emboli in both lungs, thrombus ossified lower right lower extremity branches pulmonary, edema of left foot and ankle heart normal (375 grams).

This case was grouped with the fractures of the tibia and fibula instead of with the multiple fractures (Table IV)

CASE 35 (30-749) A well nourished female, aged 33 years, fractured her right pubis 11 days before death. She also had bleeding from the right ear. She was apparently recovering until about one half hour before death, when dyspnea and cyanosis developed and her pulse became weak. Autopsy findings embolus in main pulmonary artery, thrombosed left femoral vein, ecchymoses of right elbow, shoulder, and hip, heart normal (260 grams)

This is another exception to my statement that the thrombus always develops near the site of fracture. However, it is to be noted that there was ecchymosis over the right hip and there may have been deep injury, although none was described.

CASE 36 (30-1485) A well nourished male, aged 53 years, 4 days before death, fractured his skull and suffered as well laceration of the forehead. Autopsy findings embolus in right lung, infarct of left lung, source of emboli not found, bronchopneumonia, heart normal (340 grams)

Unfortunately the source for the embolus was not found in this case. It is possible that the source might have been in a dural sinus. In this series of traumatic deaths there were 435 fractures of the skull and in 6 of these thrombi were found in the dural sinuses. These 6 may be considered as cases of potential pulmonary embolism.

CASE 37 (32-1012) An obese male, aged 60 years, fractured a vertebra, 44 days before death, and suffered abrasions of the forehead. He had pain in the neck and numbness of the right arm. Blood pressure was 150/90. X-ray examination revealed dislocation of fifth on sixth cervical vertebrae. A cast was applied. Course was uneventful. He suddenly complained of severe pain, with respirations, slow and deep, pulse, weak, no cyanosis. Cardiac type of death. Autopsy findings multiple small emboli or thrombi—source not found, heart normal (405 grams)

CASE 38 (29-1137) A well nourished male, aged 67 years, fell 11 days before death, fracturing three ribs on the left side. There was a bruise over the left greater trochanter and one on the back of the right shoulder. The chest was strapped. After breakfast he had an attack of difficult breathing and died at 9 a.m. Autopsy findings embolism of left lung—source not found, bronchopneumonia, heart, coronary sclerosis (400 grams)

CASE 39 (27-920) A fairly well nourished male, aged 49 years, was thrown from a wagon 16 days before death, and suffered fractures of the ribs on both sides, fracture of the eleventh dorsal vertebra, bruise of left breast. Subcutaneous emphysema was noted and pneumothorax. Leucocyte count was 6,250. Temperature was 99 to 104 degrees. The condition was good 25 minutes before death. Ten minutes before death he became cold, clammy, pulse less and dyspneic. Autopsy findings embolism of right lung, thrombosed left common iliac vein, heart normal (330 grams)

Here the source of the embolus was well removed from the sites of obvious injury.

CASE 40 (27-1123) A well nourished female, aged 72 years, had fractured some ribs and her right leg, 13 days before death. The tibia and fibula were plated. Death was sudden. Autopsy findings bilateral pulmonary embolism, thrombosed right popliteal vein in region of fracture, heart normal (300 grams)

CASE 41 (28-1524) Patient was a well nourished male, aged 78 years. Eleven days before death he had fractured some ribs on the right and bruised his right leg. A bruise was present in the lumbar region. The chest was strapped. Autopsy findings bilateral embolism, thrombosed right femoral vein, bronchopneumonia, heart, coronary sclerosis (425 grams)

It should be noted that there was bruising but no fracture of the right leg, nevertheless it was in this extremity that the thrombosed vein was found.

CASE 42 (29-1019) Patient was a well nourished female, aged 67 years. Six days before death she fractured the left pubis and ribs on the right. Large varicose veins were present on right leg. She was afebrile. Fourteen and one-half hours before death she went into shock. Blood pressure was 150/80. Autopsy findings bilateral embolism, thrombus milked from left lower extremity, thrombosed left common iliac vein, heart normal (350 grams)

This patient had varicose veins of the right leg but the thrombosed vein was found on the left side, fairly close to one of the sites of bone fracture.

CASE 43 (30-1063) A well nourished female, aged 46 years, had fractured her left clavicle and ribs 15 days before death. She was taken home from the hospital 4 days before death. Death was "quite sudden." Autopsy findings embolus in main pulmonary artery—source not found, heart normal (250 grams)

CASE 44. (30-1967) An obese female, aged 55 years, was injured in an automobile accident 3½ days before death, sustaining fractures of the right humerus, tibia, and ribs, laceration of forehead, bruising of both knees and right leg. A splint was applied. While splint was being removed she complained of difficulty in breathing and died in about 10 minutes. Autopsy findings small emboli in both lungs, thrombi in both external iliac veins and inferior vena cava, heart hypertrophied (520 grams)

CASE 45 (31-678) A well nourished male, aged 55 years, fell 7 days before death. The X-ray revealed fractures of left os calcis and both wrists, compression fracture first lumbar vertebra, separation of left sacro-iliac joint and symphysis pubis. Urine was bloody. He became irrational 2 days before death. Six hours before death he had sharp pain in the right chest and dullness over the middle lobe. Ten minutes before death he developed severe sharp pain beneath the upper portion of the sternum and became extremely cyanotic, with gasping respirations and engorgement of neck veins. Autopsy findings embolus in main pulmonary artery, infarct right lung, thrombosed left femoral vein, heart normal (380 grams)

CASE 46 (31-1634) Patient was a well nourished male, aged 31 years. He was injured in an automobile accident, 26 days before death, when he sustained fractures of the left scapula and 4 ribs, laceration and bruises of the scalp, with bruising of the right upper arm and the left knee. Eighteen days before death a diagnosis was made of pneumonia. There was difficult respiration and a temperature of 99 to 101 degrees. The X-ray showed a left hydropneumothorax. Sixteen days before death temperature was

100.5 degrees. Six days before death the leucocytes were 12,000. Four days before death there was sudden attack of syncope, abn. air hunger and thready pulse. Three days before death the chest was aspirated and air injected. The following day the leucocytes were 3,500. About 3 minutes before death he had abdominal pain, syncope, air hunger and then syncope. Autopsy findings: bilateral pulmonary embolism and thrombosis; emboli found in right heart and inferior vena cava, infarct of left lung; thrombus pulled from left common iliac vein, bronchopneumonia, heart normal (345 grams).

In this patient there was bruising of the left knee which may account for the thrombus which was pulled from the left common iliac vein. Where this expressed thrombus was attached is unknown.

CASE 47 (37-1403) A well nourished male, aged 67 years, was injured in an automobile accident 4 days before death. X-ray examination revealed comminuted fracture of left tibia, extending into knee joint, fracture of neck of left femur and greater trochanter, bones of left wrist, abrasions and laceration of left hip. Twenty-four hours before death temperature rose to 102 degrees. Pulse as 90 to 30. Autopsy findings: small embolus or thrombus in right pulmonary artery—source not found, lobes pneumoniae, heart normal (155 grams).

CASE 48 (33-308) A well nourished female, aged 40 years, was in an automobile accident 9 days before death with resulting fractures of pelvis, right clavicle, ribs (both sides), and bones of the right shoulder. She was getting along well. Then she suddenly became cyanotic. Autopsy findings: bilateral pulmonary embolism—source not found, heart normal (185 grams).

CASE 49 (5-703) A well nourished male, aged 38 years, was injured in an automobile accident 3 days before death, sustaining compound fractures of the left humerus and radius. He got along all right while sitting in bed, he complained of his heart, it had stopped beating. Autopsy findings: embolus in main trunk and both branches of pulmonary artery, thrombosed left basilar vein, heart normal (200 grams).

This case is of interest for two reasons: first, because all other patients dying of post-traumatic pulmonary embolism were at least 30 years of age; second, because the embolism followed fracture of an upper extremity which is rare. Whether the fact that the fractures were compound had any rôle is open to question, since in most instances of post-traumatic pulmonary embolism the fractures are not compound.

CASE 50 (37-360) A well nourished female (adult), 3 days before death, had suffered bilateral fractures of ribs and left clavicle. There was bruising of the left shoulder, knee, and both legs. Sixty-eight minutes before death she had precordial pain, cyanosis, and dyspnea. Pulse was 0. She went into shock and became cold and clammy. The temperature was subnormal. There were rales and bronchial heralding. Autopsy findings: bilateral pulmonary embolism, thrombus pulled from left leg, subarachnoid hemorrhage, heart, pericardial space obliterated (165 grams).

It is to be noted that there was merely bruising of one knee and both legs.

CASE 51 (5-445) A fairly well nourished male, aged 30 years, was in an automobile accident 11 days before death, sustaining fractures of the right leg and left ribs. In the hospital he was unconscious and had fever. Autopsy findings: bilateral pulmonary embolism, infarcts of left lung, thrombosed left iliac and femoral veins and vena cava, bronchopneumonia, heart, coronary sclerosis (gas gangrene).

This case suggests propagation of the thrombus to make it bilateral.

CASE 52 (5-67) A well nourished male, aged 40 years, fell 4½ days before death, with production of compound comminuted fracture of the lower third of the right femur and fracture of ribs on the right. A splint was applied. He got along well until 4 days before death when gas gangrene was noted. The infected tissue was excised on the day before death. Autopsy findings: embolism of left lung—source not found, heart, subacute bacterial endocarditis of aortic valve (315 grams).

Did the facts that the fracture was compound, that gas gangrene was present, and that the infected tissue was excised have anything to do with the embolism?

CASE 53 (39-300) A well nourished male, aged 36 years, 5 days before death, sustained compound fractures of right ankle and left humerus, fractures of nose and right ribs. Cellulitis of right leg developed. The ankle was operated upon on the day of death. There was septic type of temperature. The day of death the temperature was 100.6 degrees. He felt well. Symptoms of embolism appeared 70 minutes before death. Autopsy findings: small embolus left lung, infarct (?) right lung, thrombosed vein of right leg, cellulitis left lowermost muscle, edema of right leg, heart normal (300 grams).

What parts did the compound nature of the fractures and the cellulitis play in the development of the thrombus?

CASE 54 (32-1221) A well nourished male, aged 64 years, was injured in an accident 6 days before death, the injury sustained demanding amputation of the left leg at the knee. He had laceration of the right upper arm, and signs of pulmonary edema. Autopsy findings: small bilateral emboli, thrombosed left femoral vein, heart normal (165 grams).

This is classified with fractures of the tibia in Table IV.

CASE 55 (32-469) A fairly well nourished male, aged 70 years, was injured in a motorcycle accident 4½ months before death, suffering bruised face. Later nasal infection developed. Three days before death he was up and around. Suddenly he developed severe pain in the left chest with cyanosis and cough. Later there are fever and rales. Autopsy findings: bilateral infarct emboli; infarcts left lung, thrombus in postcaval phlegm, heart normal (435 grams).

One might possibly object to the inclusion of this case on two grounds: first, that the trauma is too long removed and was too slight and that the nasal infection was the most likely cause; and, second, that it should be regarded as pulmonary

thrombosis instead of embolism. These objections are difficult to deny.

CASE 56 (33 1082) An obese female, aged 50 years, received lacerations of the right forearm in an automobile accident 2 weeks before death. She had hypertension six hours before death there developed dyspnea and pain in the head, the pulse was very weak, and breathing was heavy. Autopsy findings "pulmonary embolism or thrombosis", thrombosed veins right forearm, edema of legs, heart hypertrophied (575 grams).

This case somewhat resembles Case 49, although there was no fracture.

CASE 57 (33 776) An obese female, aged 50 years, fell down stairs 16 days before death and ruptured her spleen. She was unconscious for a few minutes and semicomatose for 12 hours. There was pain in the left abdomen and flank. Abdominal distention and dyspnea developed. Systolic blood pressures were 70, 130, and 140. Twelve days before death the leucocytes were 21,500, polymorphonuclears, 74 per cent. Four days before death the temperature was normal. There was soreness of left shoulder, chest, and buttocks. Forty eight minutes before death there was sudden difficulty in breathing, gasping respirations, cyanosis, skin cold and clammy. Autopsy findings embolus in main pulmonary artery—source not found, heart, left ventricular hypertrophy (475 grams).

CASE 58 (28-1266) An obese male, aged 54 years, fell 9 days before death, scraping the calf of the right leg. There was brawny swelling and bluish discoloration of the right leg below the knee. It was treated by elevation, heat, and massage. About 24 hours before death he had difficulty in breathing and cyanosis. These lasted a few minutes. About 1 hour before death, during massage, he complained of a peculiar sensation, "His stomach turning over." This was followed by dyspnea, cyanosis, and perspiration. Pulse was very poor. About 5 minutes before death cyanosis increased. Autopsy findings embolus in main pulmonary artery, infarcts in right lung, thrombosed right popliteal vein, heart hypertrophied, myocardial fibrosis (500 grams).

Did the massage have anything to do with the loosening of the thrombus?

CASE 59 (31 1875) A fairly well nourished male, aged 70 years, was admitted to the hospital 57 days before his death with hemiplegia, senile dementia, and fracture of the left humerus. His course was progressively downhill with increasing weakness. Autopsy findings bilateral pulmonary embolism, infarcts of lungs, thrombosed left femoral vein, edema of left leg, carcinoma of stomach with metastases, heart normal (300 grams).

It was not determined whether the fracture of the humerus was a pathological one. Here again the source of the embolus was at a distance from the site of trauma. It might be argued that the debility from the hemiplegia and the carcinoma were of as great importance as the fracture in causing the thrombosis and subsequent embolism.

CASE 60 (31 1110) A poorly nourished female, aged 39 years (Three months before death she had an oophorectomy.) She was injured in an automobile accident 36 days before death. Shortly afterward there was abdominal pain. Thirteen days before death, a diagnosis was made of

intestinal obstruction and the following day laparotomy was done. Progressive downhill course was noted. Autopsy findings "bilateral pulmonary embolism or thrombosis" (partially adherent), infarct right lung, thrombosed right common iliac and uterine veins, wound infected, carcinoma of stomach, heart normal (200 grams).

There are some objections to including this as an instance of post-traumatic embolism. It is not clear why the accident was followed by abdominal pain. There was no clue in the record as to the injury sustained. Perhaps it might be argued that the laparotomy was of more importance than the trauma.

CASE 61 (33 1012) A fairly well nourished male, aged 57 years, was stabbed in the abdomen 112 days before death. Laparotomies were done on the one hundred and twelfth, sixty ninth, forty third, and second days before death. He failed rapidly after the last operation. Autopsy findings "bilateral pulmonary embolism or thrombosis"—source not found, heart normal (295 grams).

Objection may also be made to including this case as an instance of post-traumatic embolism. It might be stated that a stab wound of the abdomen should be included with laparotomies, especially since there were no other injuries. The four subsequent laparotomies may have been of more importance than the trauma. Objection might also be made on the basis that this was an instance of pulmonary artery thrombosis instead of embolism, since no source for an embolus was found.

These cases and the controls are summarized in Tables IV and V. The most striking thing in Table IV is the high incidence of embolism after fractures of the long bones of the lower extremities. This is probably due to several factors.

1. Fracture of the femur is an affliction of advanced age. Of the 118 fatal fractures (1 a dislocation) of this bone 108 were in persons of 50 years of age or over. This is not quite so true of fracture of the lower leg, although 28 of the 39 individuals were 50 years of age or older. Eighteen of the 31 individuals with fracture of the pelvis were 50 or more years of age. Sixteen of the 25 persons with fractured arm were 50 years of age or over. Thirty of the 68 cases with fracture of the spine were 50 years of age or more.

2. Fractures of the lower extremity but especially of the femur require more prolonged rest in bed and stricter immobilization than fractures elsewhere.

3. There is a high incidence of anatomical cardiac disease, which was as follows: femur 45 per cent, leg 28 per cent, pelvis 29 per cent, arm 28 per cent, and spine 14 per cent. If consideration is given only to those over 50 years of age these figures become, femur 49 per cent, leg 32

per cent pelvis 44 per cent arm 37 per cent and spine 23 per cent. This does not mean that all or even a large part of these persons had any clinical evidence of cardiac disease, but that many may have had a potential impairment of their circulation. In this series of 61 embolic deaths, anatomical heart disease was present in 22 cases or in 36 per cent, which is a higher incidence than for the traumatic group as a whole (20 per cent).

4. It is well known that there is a decided tendency for the source of pulmonary emboli to be found in the veins of the lower extremities and pelvis. It is obvious that the trauma to soft tissues attendant on fracture of the long bones of the lower extremity may readily bruise or lacerate the veins in this region, giving excellent possibilities for the development of thrombi on the injured endothelium. Mention has already been made of the possible but unproven rôle of varicose veins.

In addition to the foregoing, other at present unknown factors may play a part.

In a former paper I called attention to the fact that post-traumatic embolism tends to occur later than postoperative and post-partum embolism. This is further shown in Table V wherein 31 of the embolisms took place after the second week and 15 after the fourth week.

The part played by operative procedures secondary to the trauma sustained is indeterminate. It is probably true that valid objections might be made to the inclusion of some of these cases as embolisms, but I feel that they all help to make impressively the frequency of thromboembolic disease of the lungs as a result of trauma.

In my former paper certain general conclusions were drawn, which require only slight modifications at this time:

1. (a) Post-traumatic thrombosis and embolism are rather common. In fact embolism is more common following trauma than after conditions not involving trauma. (b) Embolism following trauma is decidedly more common in females than in males.

2. The source of the embolus is usually at the site of injury.

Further it may be concluded:

1. Fatal fractures of the lower extremities are afflictions of advanced age.

2. Fracture of the femur or leg is the most common cause of post-traumatic pulmonary embolism.

3. The prolonged immobilization and rest in bed necessary for repair of fractures of the long bones of the lower extremity promote stasis and the possibility of a resulting thrombosis. It is to be noted that in 35 of the 61 cases there was a

fracture of the lower extremity and that in the remaining 26 cases there were fractures or bruises of the lower extremity in 13.

4. The trauma to vessels by fractures gives an ideal site for the initiation of thrombosis.

5. Injuries requiring less degrees of enforced inactivity are only rarely followed by pulmonary embolism.

6. Age, heart disease and time of death do not explain the sex difference in incidence of pulmonary embolism following trauma.

7. The incidence of anatomical heart disease is significantly higher in persons dead of post-traumatic pulmonary embolism than it is in persons dead of trauma without embolism.

#### SUMMARY

Sixty-one cases of pulmonary embolism following trauma are reported. These represent more than 20 per cent of the deaths due to pulmonary embolism in a series of 9,781 necropsies. In about 80 per cent of these post-traumatic pulmonary embolisms there was injury of a lower extremity usually a simple fracture. Pulmonary embolism is rare after fractures of bones other than those of the lower extremity. Embolism following trauma is decidedly more common in the female than in the male. This sex difference is not to be explained on the basis of age, the incidence of heart disease or the time of death following the injury. It is suggested that the higher incidence of varicose veins in the female may be responsible.

Since this paper was prepared Vance has reported 60 cases of pulmonary embolism following trauma. Of his 60 cases 45 involved injury, chiefly fractures, of the lower extremity. (Vance, B. M. Thrombosis of the veins of the lower extremity and pulmonary embolism as a complication of trauma. *Am J Surg*, 1934, 26: 9-26.)

#### BIBLIOGRAPHY

- BRUNS, P. *Westens Beiträge zur Fracturheilkunde*. 3. Ueber plötzliche Todesfälle nach Knochenbrüchen in Folge von Venenthrombose und Embolie. *Beitr. Klin. Chir.*, 1886, 1-8.
- DAVIS, S. Ueber traumatische Thrombose. *Deutsche Arch. f. Klin. Med.*, 9: 2, 348-368.
- HEDENHÖJ, E. F. Fatal pulmonary embolism: statistical review. *Arch. Surg.*, 1927, 5: 4, 536.
- HÖRSTEMANN, F. O. Ueber die Zusammenhänge zwischen Lungenembolien und ihren Ursachen. *Deutsche Zeitschr. f. Chir.*, 1928, 207: 360-379.
- KELLER, H. *Todesfälle Lungenembolie bei der Freiburger Chirurgischen Klinik*. *Klin. Wochenschr.*, 1930, 9: 730-736.
- LEITCH, W. A. A statistical investigation into the causation of pulmonary embolism following operation. *Lancet*, 1927, 1: 6.
- LOTHMEYER, O. Zur Embolie der Lungenarterie nach Verletzungen und operativen Eingriffen. *Beitr. Klin. Chir.*, 1903, 3: 633-686.

- 8 McCARTNEY, J S Pulmonary embolism, a report of seventy three cases Arch Path, 1927, 3 921-937
- 9 MCPHEETERS, H O Varicose Veins 3d ed, 1931, pp 39-40 Philadelphia F A. Davis Co, 1931
- 10 MARTINI Ueber die Zunahme der Thrombosen und toedlichen Lungenembolien Arch f klin Chir, 1928, 153 495-514
- 11 MILLER, A H, and ROGERS, H. Postoperative embolism and phlebitis J Am M Ass, 1929, 93 1452
- 12 ORATOR and STRAATEN Zur Klinik der postoperative Infarktpneumonien Klin Wchnschr, 1930, 9 740
- 13 SARAFOFF, D Thrombosen und Lungenembolien Leipziger Chirurg Univ -Klinik für das Dezennum 1920 bis 1929 Arch f klin Chir, 1930, 161 493-501

## TREATMENT OF THE ATONIC BLADDER<sup>1</sup>

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THE terms "atonic bladder" or "cord bladder" are generally accepted as referring to a condition of incompetence of the detrusor muscles of the bladder resulting from abnormal innervation. Although atony of the bladder is always secondary to some extravascular lesion, when it occurs as the result of disease affecting nerves supplying the bladder, it may, from a clinical standpoint, be regarded as primary. If this were granted, atony of the bladder resulting from obstruction at the vesical neck might be regarded as secondary. In some cases both obstruction and abnormal innervation are involved.

Although the function of the nerves involved in micturition and the mechanism of micturition are not exactly known, theories have gained general acceptance in which the parasympathetic or sacral nerves are regarded as contracting or emptying nerves, and the sympathetic or pre-sacral plexus in control of the internal sphincter is regarded as a group of filling nerves. Impairment of the parasympathetic or emptying nerves will cause retention of urine.

The exact manner in which the so called internal and external sphincters of the bladder and urethra function during micturition is still undetermined. The internal sphincter is composed of smooth muscle and is supposed to be in a state of tonic contraction, relaxing automatically on the emptying of the bladder. Only when the pressure of overdistention becomes great enough is the contracted status of the sphincteric muscle overcome. The function of the internal sphincter was first regarded as of little importance, for it was shown that its destruction, which frequently occurred in suprapubic prostatectomy, was not followed by any disturbance in micturition or in control of the bladder. It was evident that the external sphincter sufficed to prevent incontinence. However, in recent years the part played by the musculature involved in the so called

vesical neck, and generally referred to as the internal sphincter, has assumed greater importance. It is now recognized that unless the internal sphincter, and particularly its dorsal portion, is completely relaxed, micturition is impeded and retention of urine will result. Inability on the part of the sphincter to relax has been called dysectasia. Failure of co-ordination of the muscles that are situated at the vesical neck and that are involved in micturition has also been considered to be a factor in causing retention. Such inco-ordination has been called achalasia. Although it is possible that such dysfunction is closely related to dysectasia, and that the two result from similar causes, yet retention of urine is occasionally observed when the internal sphincter may appear to be normal, and when there is no gross evidence of fixation.

Sphincteric dysfunction may result from a variety of causes which may be roughly grouped under the headings of mechanical and neurogenous. Mechanical fixation of the sphincter may result from cicatricial changes in the sphincteric and perisphincteric tissues secondary to chronic infection. This is well illustrated by the retention of urine that so frequently is observed with a so called contracted vesical neck, often the sphincter is involved in cicatricial tissue so that it is unable to relax. Although prostatic hyperplasia may cause retention of urine as the result of obstruction in the prostatic tissues, the coincident sphincteric rigidity is probably a greater factor.

As the result of either chronic sphincteric dysfunction or mechanical obstruction, secondary atony of the detrusor muscles may develop. With marked retention of long standing, the atony may become so extensive that, although the obstruction is removed, contractile power returns only in part. Various methods have been attempted to determine the remaining degree of contractile power in the detrusor muscles, as

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Fig Typical round, smooth outline of atonic bladder

well as the possibility of their becoming rehabilitated. Cystometric studies have been carried out by various observers, with varying degrees of success. Rose has maintained that the cystometer, if its readings are correctly interpreted, will give a valuable index to the actual and potential status of the detrusor muscles. It has been our experience that although cystometric data are often of corroborative value, they frequently fail to give the definite information desired. Another index to the potential contractile power of the detrusor muscles may be derived from injection of acetylcholine or mecbolin. If the expulsive force of the bladder is definitely increased as the result of such injections, it is possible to assume that contractile power eventually will improve.

In recent years, we frequently have observed an interesting condition characterized by marked atony of the musculature of the bladder with chronic retention of urine, in which evidence of prostatic obstruction could not be discovered on rectal examination or by cystoscopy and in which physical examination, including examination of the nervous system, gives negative results. When the catheter is introduced, marked reduction in expulsive force is evident. A cystogram may give an outline that is typical of so called tonic bladder (Fig. 1) that is, there is a smooth, round outline instead of the irregularities of trabeculation usually observed with obstruction. On cysto-urethroscopy the wall of the bladder will appear to be flabby and distended, with no trabeculation or other evidence

of obstruction. Careful inspection may however disclose evidence of cicatricial changes, with more or less contracture or lack of elasticity of the tissues of the internal sphincter and vesical neck. In other cases there may be slight hyperplasia of the sphincteric tissues. These conditions may be easily overlooked unless carefully observed, and in some cases it is necessary to use a retrograde lens. The tissue present is usually not enough to cause actual obstruction, but it apparently interferes with the physiological relaxation or co-ordination of the internal sphincter so as to cause urinary retention.

In treatment of this condition, an attempt should be made to remove the cicatricial or hyperplastic tissues at the neck of the bladder. The direct vision punch has proved to be admirably adapted to this purpose. It is frequently surprising how little tissue it is necessary to remove often not more than a gram or two, to bring about the desired degree of relaxation. In order to restore vesical function, it will be necessary to remove every bit of abnormal tissue which can be seen in any portion of the vesical neck, so that it is smooth and on an even surface with the mucosa of the bladder.

The return of function of the musculature of the bladder is often slow and several weeks or months may be required after operation before function is fully restored. Following operation it may be necessary to leave a retention catheter in the bladder for several days, and in some cases it is necessary to perform intermittent catheterization for several weeks. It will be seen that the intervals of catheterization will increase and the amount of residual urine will decrease, as the contractile power of the bladder returns. During the interval of recovery intramuscular injection of acetylcholine has, in some cases, seemed to act as a nerve stimulant. Occasional instillation into the bladder of 1 ounce (30 c.c.) of 1 per cent to 0.2 per cent of an aqueous solution of gentian violet also will hasten the desire to void. In a few cases, complete relaxation of the sphincter is exceedingly difficult to accomplish. In some cases, relaxation is aided by postoperative dilatation, at regular intervals, with a Kollman dilator expanded to as much as 40 or 45 French. In an occasional case spastic condition may persist, justifying resection of the premeatal nerves in an effort to overcome the neurogenous imbalance.

In the past 5 years we have observed 24 patients with atonic bladder of this type. Function of the bladders of 20 of these was completely restored by the freeing of the internal sphincter of cicatricial or hyperplastic tissue, by the use of

the transurethral punch In 3 cases, although retention was overcome, complete normal function was not restored In 2 cases, permanent normal function was established after resection of the presacral nerves In case no abnormality of the internal sphincter can be discovered, evident failure of co-ordination may be remedied

#### ATONIC BLADDER IN THE FEMALE

Because of differences in structure of the sphincter of the bladder in the two sexes, problems related to atony of the bladder in the female, are quite different from those related to the corresponding condition in the male Although the sphincter has been described as consisting of external and internal fibers, still, from a functional standpoint, there is but a single sphincter Atonic bladder in the female may result either from neurogenous or mechanical factors, or both When innervation of the bladder is involved, the lesion may be localized either to the central nervous system or to the terminal nerves With atony resulting from a lesion of a nerve, marked relaxation of the sphincter, and incontinence, are observed much less frequently in the female than in the male The sphincter may be relaxed on urethroscopic examination, but sufficient contractile power remains, aided by accessory muscles, to prevent much, if any, leakage Sympathetic neurectomy may be indicated as long as the sphincter is continent, and some contractile power of the detrusor muscles remains The imbalance between the sympathetic and the parasympathetic innervation, as it affects the vesical sphincter, is usually not as marked in the female as in the male, yet marked increase in expulsive force has been observed in several so called atonic bladders following presacral neurectomy

Mechanical factors involving the sphincter usually result from hypertrophy, cicatrization, or tumor As a result of such obstruction, secondary atony of the musculature of the bladder may follow, from which complete recovery may be slow and is not always possible, even though obstructive factors are eliminated Hypertrophy of the sphincter, causing retention of urine and secondary atony, is frequently observed It may be due to nervous imbalance or to hyperplasia Although it may not be easily recognized, as a rule evidence of sphincteric hyperplasia is visible on urethroscopic examination When either of these factors is evident, incision into the sphincter, with forcible dilation, often will correct the condition It has been our experience that in most of these cases it is necessary to remove several pieces

of tissue from different portions of the sphincter, before sufficient relaxation of the sphincter can be secured The danger of secondary insufficiency, with slight incontinence, must be risked, but usually this is overcome as the sphincter recovers its tonus Intermittent catheterization may be indicated for a variable period following sphincterotomy, in order to help restore the tonus of the vesical wall What is accomplished is not removal of actual obstructing tissue, but correction of sphincteric dysectasia, with restoration of sphincteric relaxation

#### MISCELLANEOUS TYPES OF ATONY

Atony of the wall of the bladder may result from injury to branches of the pelvic nerves, caused in the course of operations on the bladder, lower part of the ureter, or rectum We have observed such atony occurring in 2 cases following ureterectomy, with extensive resection of the adjacent portion of the vesical wall Evidence of atony was localized to the adjacent portion of the bladder but was sufficient, in one case, to cause 150 cubic centimeters of residual urine Subsequent compensatory hypertrophy of the intact neuromusculature reduced this to 30 cubic centimeters It was very evident that in the course of the resection important parasympathetic fibers had been cut

Atony of the bladder was frequently observed several years ago, following the Kraske type of operation for resection of the sigmoid It was very evident that sacral nerves controlling the detrusor muscles of the bladder were sometimes destroyed in the course of the operation In most instances the wall of the bladder recovered its contractile powers, at least in part In other instances, the atony remained permanent In recent years, modifications in the technique of posterior resection of the sigmoid have been made, which have largely obviated such injury to nerves When injury occurs, intermittent catheterization or suprapubic drainage should be instituted without delay

Amounts of residual urine, varying from 30 to 100 cubic centimeters, are occasionally observed in the presence of clinical evidence of senility, although no definite lesion can be demonstrated on examination of the nervous system Rectal examination and cysto-urethroscopy may also fail to demonstrate any cause for the residual urine Largely by exclusion, it would seem logical to infer that a lesion exists in the structures that innervate the bladder, related to the arteriosclerotic or senile changes existing in the central nervous system





Fig. 2. Pyeloidal outline of bladder frequently seen with obstruction. Irregularities are caused by trabeculation and cellules.



Fig. 3. Another outline of the bladder seen with obstruction. Irregularities are caused by trabeculation, cellules, and by diverticula.

So called hysterical retention of urine is often observed, although curiously not so often as in former years. In most cases it is apparently caused by a spastic condition of the sphincter of functional origin, although secondary atony of the wall of the bladder may be noted in cases of long standing. Absence of the reflex pain that usually is observed with overdistention of the bladder is a curious feature, and must be explained on the basis of hysterical diminution in sensation.

In the treatment of atonic bladder with evident imbalance of sympathetic and parasympathetic innervation, before considering presacral neurectomy Learmonth has advised preliminary exploration of the lower vertebrae if there is any doubt as to the existence of vertebral or spinal abnormality. In some of these cases no somatic evidence of a neurogenic defect can be obtained. Among the local compressing agents are tumors, cartilaginous bands, meningocele and bony spurs. Removal of such structures will, in favorable cases, permit restoration of normal function. When imbalance of innervation is marked by accentuation of the hypogastric influence presacral resection has resulted in restoration, or marked improvement, of normal function in a sufficient number of our cases to demonstrate its practical value. The indications laid down by Learmonth, for operation for neuromuscular imbalance are as follows: (1) clinical data must

point to reduction of function of the pelvic nerves, but sufficient function must remain to permit some contraction. (2) the hypogastric nerves must be uninjured. In other words, it is inferred that the balance of visceral innervation is disturbed, and injured pelvic nerves are handicapped in their task by the braking action of normal hypogastric nerves. However there must not be total paralysis in the distribution of the pelvic nerves, for after the brake is removed, the residual expulsive force of the detrusor muscles must become equal to emptying the bladder. In addition, the patient must be continent and must have no impairment of the external sphincter muscle and finally renal function must be satisfactory.

Presacral neurectomy is, unfortunately, not applicable in the majority of cases in which there are lesions of the central nervous system, such as there are in tabes. However when the external sphincter is intact, and some residual contractile power remains in the detrusor muscles, presacral neurectomy may be considered. The atonic condition of the bladder of many tabetic patients will improve following antisyphilitic treatment, particularly if treatment includes intermittent catheterization. The amount of residual urine perhaps originally large will be greatly reduced by such treatment and in some cases all residual urine will disappear. It is of interest that atony of the bladder secondary to tabes occurs much less

frequently in the female Presacral resection is rarely possible as a means of treatment of paralysis of the bladder following traumatic injury to the spine. As a rule, the contractile power of the detrusor muscles is completely lost, and even though the sphincter is intact, much cannot be expected from overcoming the braking influence of the sympathetic nerves.

The non surgical treatment of atonic bladder is of considerable importance. Particular emphasis should be laid on drainage. We are inclined to agree with Cabot, that in every case in which acute retention occurs after operation or as the result of obstruction, the catheter should be employed to drain the bladder before its normal capacity is exceeded. Early and repeated catheterization will prevent renal infection better than any other measure. Whether or not suprapubic drainage is done is of secondary importance. The main objective is to prevent overdistention of the bladder. However, with injuries to the spine resulting in paralysis of the bladder, the conditions are quite different. The atonic condition of the vesical musculature will not, as a rule, cause sufficient renal back pressure to injure the kidneys or ureters. Furthermore, congestion and trauma to the bladder itself as the result of retention will not follow to the extent observed with intact vesical musculature. Overflow of the bladder usually will be established, and there is much less danger of ascending infection than would occur after catheterization. Recommendations that the bladder be allowed to overflow rather than that the catheter be used, have been previously suggested by a number of observers, including Plaggemeyer, Wesson, and Cabot.

Chronic retention of urine resulting from an atonic bladder seems to have quite different results, and produces a different cystographic picture (Figs 2 and 3) than the chronic retention seen in most cases of obstructive retention. Instead of impairment of the ureterovesical protecting mechanism, and impairment of ureteral peristalsis, together with reflux of vesical content often as far as the renal pelvis, such as frequently occurs in the presence of obstruction, the quite different picture seen in the presence of vesical atony, is slowly increasing residual urine and vesical decompensation. Apparently the ureterovesical barrier, and ureteral peristalsis adjust themselves to the degree of impaired contractile power of the detrusor muscles, so that little or no ureteral reflux occurs. Only when ascending ureteritis has impaired the function of the lower part of the ureter will this result. It is surprising

how often patients are observed who have had atony of the bladder of varying degrees for many years, without evidence in the urogram of reflux or of any impairment of the lower part of the ureter or of the kidneys.

Patients frequently are observed who have insidious, progressive urinary obstruction, and whose bladders are so distended that they reach the upper part of the abdomen. In one case, recently observed, the mass suggested a pancreatic cyst, but fortunately catheterization proved its nature and prevented abdominal exploration. Not only are such patients singularly free of fever and chills, which ordinarily accompany intermittent or acute prostatic obstruction, but as a general rule they give no evidence of retention of urea, are often unaware of any particular urinary difficulty, and if a catheter has not been passed prior to their admission, the urine will be found negative on microscopy. The lack of renal injury in such an instance can be attributed to decompensation taking place in the detrusor muscles rather than in the ureterovesical mechanism. At any rate, lack of hypertrophy of the vesical wall has protected the kidneys.

#### SUMMARY

Atony of the bladder is never primary. It is caused either by abnormal innervation, by obstruction, or by both factors. However, for the purpose of clinical differentiation, atony resulting from disease affecting the innervation may be regarded as primary. Continuous retention of urine from any cause will produce atony of the vesical wall. In some cases it may be difficult to determine which factor is involved. With most cases of atony, obstruction, either primary or secondary, is the predominating factor.

The factors involving sphincteric dysfunction are (1) imbalance of innervation, with predominance of the sympathetic or filling nerves, (2) rigidity or failure of adequate relaxation of the internal sphincter referred to as dysectasia, and (3) apparent failure of co-ordination of reflexes involved in the act of micturition centering in the vesical neck, to which the term achalasia has been given. The first condition can be favorably influenced by presacral neurectomy, and the second condition usually can be remedied by thorough transurethral resection. Knowledge concerning cases in which other causes are operative, is insufficient as a basis from which to determine treatment, but in one case of this type, presacral resection restored function to normal.

The abnormal tissue, which interferes with function of the vesical neck may in some cases be

easily overlooked. It is necessary to remove such tissues completely and to free every clonitric contraction in order to restore sphincteric function. Sphincteric abnormality in the female presents problems quite different from those offered by corresponding conditions in the male. In most cases, judicious removal of sphincteric tissue will overcome retention, but subsequent presacral neurectomy may be necessary. Localized or partial atony may follow destruction of branches of the pelvic nerves in the course of a bladder operation. Various other types of atony may occur.

With acute retention such as often occurs following abdominal operation the advisability of drainage of the bladder before it becomes overdistended should be emphasized. In contrast, with retention following extensive injury

to the spine, overflow of the bladder should be permitted rather than catheterization.

It is evident that much still remains to be discovered in the mechanism of micturition and concerning the various lesions which may affect it.

#### BIBLIOGRAPHY

- CABOT H. *On Personal communication to authors*  
 LEARMONTH J. R. and BRAUER, W. I. Resection of the presacral nerve in the treatment of cord bladder. *Surg. Gynec. & Obst.* 1925, 5: 494-499.  
 2. FLECKENSTEIN, H. W. A case report on fractures of the spine in relation to changes in kidney and bladder function. *J. Urol.* 1925, 6: 83-93.  
 4. ROSS, D. K. and DICKINSON, ROBERT. The cystometric diagnosis of central nervous system syphilis, new appreciation of the term neurogenic bladder. *Am. J. Syphilis*, 1920, 5: 37-39.  
 5. WATSON, J. B. *Personal communication to authors.*

## TRAUMATIC OSSIFYING PERIOSTITIS OF THE NEWBORN

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A NEW type of birth injury is herewith presented with illustrative cases, because it is a frequent possibility in the practice of every physician doing obstetrics. A review of the literature does not disclose any previously reported injuries similar to these. Due to the relatively late appearance of the X-ray diagnosis, this type of birth injury probably has been overlooked often. Consequently, the cause of pain, limitation of motion, swelling and discoloration of the injured part, which are the chief clinical findings, has been attributed to injury of soft tissues only. As the reported cases illustrate, recovery is spontaneous and the patient requires no special treatment other than the application of external heat and the prevention of contracture.

## CAUSE OF INJURY

In studying this series, all of which were breech extractions, we have concluded that the injury is probably due to (1) too strong traction on the extremity, (2) a twisting pull on the leg due to the inability on the part of the accoucheur to rotate the line of traction with the rotation of the fetus as it accommodates its large diameters to those

of the birth canal, (3) the inability of the accoucheur to bring down both feet so that traction may be equally distributed, and (4) the too hasty attempt to complete the delivery. The injury to the humerus resulting because the arm was extended alongside the head calls attention to the danger of such delivery of the arms.

When version and extraction is chosen as the method of delivery, it is often done at a most unpropitious time, that is, after the membranes have ruptured and as a court of last resort. Strong traction then becomes necessary.

## INTERESTING FEATURES

Several interesting features may be noted in this group of cases. Immediate X-ray examination is negative. The calcium deposit becomes visible only after 1 or 2 weeks. Recovery takes place spontaneously, in all the cases which we have observed. Recovery time seems to be in direct proportion to the extent of the injury—4 to 12 weeks in our series—and no permanent disability has resulted. Two cases were followed until they walked.

## PATHOLOGY

A tearing or stripping of the periosteum of the femur or humerus occurs most often at its weak-



Fig 1 Case 1 First examination baby 40 days old. The left femur shows considerable elevation of periosteum in the upper part and slight elevation in upper and middle thirds of the shaft. The space between the periosteum and cortex at the upper extremity is filled with periosteal new bone formation.



Fig 2 Case 1 Second examination, baby 4 months old. The left femur shows considerable absorption of periosteal new bone shown in Figure 1.



Fig. 3

Fig. 3. Case 1. First examination, 3 day after birth. No evidence of fracture, dislocation, or pathological condition.

Fig. 4. Case 1. Second examination, baby 25 days old. The right femur shows considerable stripping of periosteum of entire circumference of shaft. The space between peri-



Fig. 4

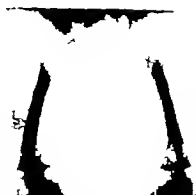


Fig. 5

osteum and cortex is filled with periosteal new bone for months.

Fig. 5. Case 1. Third examination, baby 4 months old. The right femur shows considerable absorption of periosteal new bone shown in Figure 4.

est point of attachment, the epiphysis, and the maximum strain of the traction is imposed upon the proximal epiphysis. If the trauma is more severe, we observe that the stripping follows down the shaft with further subperiosteal hemorrhage as in Case 2.

#### DIAGNOSIS

Diagnosis is important and difficult until one has followed through a case. Osteomyelitis and epiphysitis were both suggested on our first case. Fracture was the opinion of one roentgenologist. Sarcoma was also considered. In truth the lesion is similar to myositis ossificans, which has its etiology in some instances, at least, in torn periosteum. A rapid proliferation of the periosteal

osteophytes takes place with deposit of calcium. One must keep in mind that this X-ray visible periosteal injury is but part of the hemorrhage from muscle and fascial tearing.

#### SUMMARY

1. A new type of birth injury connected with breech delivery is described.
2. Roentgenograms taken from 7 to 24 days after birth would show this to be a common injury from breech extraction.
3. Essential lesion shown in the roentgenograms



Fig. 6. Case 2. First examination, baby 5 days old. The pelvis and femora show no evidence of fracture, dislocation, or pathological condition.



Fig. 7. Case 2. Second examination, baby 24 days old. Left femur shows considerable elevation of periosteum of upper extremity and slight elevation of upper and middle thirds of shaft. The space between periosteum and cortex of the upper extremity is filled with periosteal new bone formation.

is an ossifying periostitis about the proximal epiphysis

4 Treatment is not specific and recovery is spontaneous without disability

#### CONCLUSION

Too much traction on the legs or arms during breech delivery may cause extensive muscle and periosteal injuries resulting in ossifying areas

#### CASE HISTORIES

All babies were born in the Hackensack Hospital, Hackensack, New Jersey, all were first babies, all breech deliveries

1 Baby M, No 31557 The child was born December 3, 1932, labor was prolonged—posterior position. Delivery was accomplished by podalic version and breech extraction. It was noted that "the child was delivered without injuries" but it did not breathe well. It was placed in a respirator for one half hour. The child left the hospital in good condition. The trouble with its leg was first noticed about 6 weeks after birth. The right thigh was kept flexed. Motion was painful. An X ray picture on January 12, 1933, showed the peculiar calcium deposit around the epiphysis of the neck of the right femur. The family was greatly disturbed. Two orthopedic men said that there was a fracture and that the leg should be put up in a cast. Another said that the condition was an inflammatory one and should be left alone. No treatment was given and the condition cleared up entirely. X ray examination 3 months later (Fig 2) showed that the proliferative process had entirely disappeared.

2 Baby S, No 31870 The child was born December 26, 1932. The child was in frank breech position. Labor pains became ineffectual. It was necessary to grasp the foot to create traction. The head was caught on the perineum. Forceps were applied. The baby weighed 6 pounds, 15 ounces, it was 21 inches long and across shoulders 14½ inches, the head measured 15 inches. The second day it was noted that the right thigh was swollen, tender, and was held in abduction. X ray film (Fig 3) was taken on December 29, 1932, and was negative. It was noted that while baby moved right leg a little, it seemed as though it was partially paralyzed. Motion caused pain. The condition slowly improved without special treatment. An X ray examination on January 24, 1933 (Fig 4) showed large area of calcification in what must have been an extensive subperiosteal hemorrhage. After 3 months the leg was practically normal. X ray film on February 20, 1933 (Fig 5) showed much less subperiosteal deposit.

3 Baby A, No 32549 The child was born February 25, 1932. It was in posterior position. The mother's pelvis was small. Delivery was very difficult and was accomplished by podalic version and breech extraction. The mother went into obstetrical shock from which she rallied slowly. The baby weighed 6 pounds 12 ounces, its length was 22½ inches, shoulder width 14 inches, the head 14 inches. The day after birth it was noted that the left leg and foot were edematous, discolored, and caused pain when moved. X ray examination on March 2, 1932 (Fig 6) showed no pathological condition. The baby remained in the hospi-



Fig 8, left Case 4 First examination, baby 9 days old Left humerus shows moderate elevation of periosteum of external surface of upper extremity, with slight periosteal new bone formation

Fig 9 Case 4. Second examination, baby 14 days old Left humerus shows moderate elevation of periosteum of external surface of upper extremity with moderate periosteal new bone formation

tal 4 weeks. The swelling and pain began to diminish after the first week and the child gradually used the leg more. An orthopedist on March 13, 1932 suggested that the condition was essentially a nerve injury. The leg improved but on discharge March 23, 1932, a roentgenogram (Fig 7) showed the large amount of osseous formation about the upper epiphysis of the femur. Follow up at home reports that the child recovered completely.

4 Baby H, No 35508 The child was born December 6, 1933, after a prolonged labor. It was in frank posterior position. Manipulation was difficult. Delivery was accomplished by podalic version and breech extraction. There was a third degree laceration and severe postpartum bleeding. The left arm was delivered in extension alongside of the face. There was an injury to the left shoulder and arm which was noticed immediately after birth. The arm was limp and there was some wrist drop which was thought to be a nerve injury. The child weighed 8 pounds 14¾ ounces, was 22 inches in length, head measured 14 inches and shoulders 17 inches. On the second and third days it was noted that motion of his shoulder was painful and that the area around the deltoid was slightly swollen and tender. A roentgenogram was taken on December 15, 1933 (Fig 8) and showed an area of subperiosteal hemorrhage about the epiphysis of the upper extremity of the left humerus. A second X ray film on December 20, 1933 showed more calcification of same area. During the period in the hospital the child's arm improved steadily. The wrist drop disappeared and motion and strength of the arm returned although there was a tendency to hold it in a typical Erb's palsy position. Since discharge baby has recovered complete function.

# A CONSTRUCTIVE CRITICAL ANALYSIS OF MAXILLARY SINUS SURGERY

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THE surgical anatomy of any particular part of the human mechanism is the foundation upon which the success of a mechanical procedure depends. This statement is not intended to detract from the value of other known basic principles of medicine. The maxillary antrum, a cavity in the superior maxillary bone, varies in size and shape. It is the result of an invasion of the respiratory mucous membrane during life (4). Though modified it retains much of the basic character of the respiratory structure. If this presentation savors somewhat of the critical, its object is constructive, with an attempt to analyze the subject presented in a fair, just, and impartial manner. It deals with the applied surgical anatomy. The chemistry, physiology, pathology and bacteriology will be mentioned only as correlating influences.

Drainage in the presence of erosive purulent infection is a surgical axiom. It is especially referable to acute infection. Its application is at times modified by chronicity. In that these resources have in a measure fulfilled the necessary need. This is not an uncommon clinical observation. The non-surgical treatment of empyema of the antrum has been advised ( ).

The trend of maxillary sinus surgery during the past 3 decades has been the so called radical method. A better description would have been one using the term complete. It has been manifested by the usual concomitant enthusiasm many times far beyond its real merit and value. In this the writer assumes his full share of responsibility (16). Though much has been published on the surgery of the maxillary sinus, the greater portion of these observations has been referable to the histopathology of the mucous membrane. Little has been presented on the surgical anatomy. Whether the trend to rely upon the X-ray has been a factor the writer is unable to state. It would seem that the surgical anatomy of this structure is a closed book and that little new may be added by investigating this particular aspect of the subject. From a series of observations, the writer has assumed a somewhat different attitude than he formerly held.

In this presentation, two principles involved in radical maxillary sinus surgery are discussed. They are first, the histological fact that the mucous membrane of this structure normally

possesses cilia sweeping its contents toward the natural ostium, that this ciliary activity varies from that of a kinetic action to one of inaction with a potential reserve, depending upon the degree and type of pathology present; second, a series of anatomical observations and their surgical application. Beyond the realm of these two principles, this presentation is not concerned. It is assumed that a final clinical result is the object sought in any method of therapy. Changes in the mucosa, the presence of foci, their relation to systemic invasion and disturbances must be weighed in the final analysis of clinical observation.

Ciliary activity of the respiratory mucous membranes has been studied by innumerable observers. McDonald and his co-workers draw certain conclusions, one of which is that by way of ascription their work points directly to the existence of neural, chemical, and physical control mechanism for regulation of the rate of ciliary activity in higher vertebrates. Their observations are the result of much animal and pharmacological experimentation. They quote freely from the opinion of others. Bloomfield states: "In a study of the etiology of respiratory infections, we have in the past overemphasized secondary factors, such as identification of the offending organisms and the determination of its mode of transposition to the human host, but have neglected the most essential factor, namely the respiratory surface itself. It is only when some abnormal change or injury occurs in the host, that colonization and invasion occurs. Our ciliated surfaces do not become infected whenever pathogenic microorganisms gain access to them. This is a matter of common observation. It has been demonstrated experimentally that when many types of pathogenic bacteria are brought into contact in large numbers with the upper respiratory mucous membrane of healthy persons, these microorganisms are easily disposed of within a very short time without colonization and invasion (1,5). These principles apply to other structures of the body as well. I refer to the gastro-intestinal tract, fallopian tubes, and male urethra."

Small gross sections of mucous membranes removed from infected antra, both acute and chronic when placed upon a warm microscopic stage clearly demonstrate ciliary activity. The writer



Fig 1 Frontal section through both superior maxillæ in the plane of the anterior one third of the inferior turbinate. It shows at A and A' the maxillary sinus and floor, B and B' the inferior turbinate, C and C' the nasal floor, D the nasal septum, E and E' the inferior conchal crest. Notice the difference in the corresponding levels of the nasal and maxillary sinus floors

has made such observations, and has seen it demonstrated in the laboratory of the Massachusetts Eye and Ear Infirmary under the direction of Dr Harris P Mosher. This ciliary activity varies. It may be sluggish, nevertheless it is usually present. Proetz states "The fact that normal ciliary activity persists in the presence of even the worst sinus infections demands a new conception of the mechanism of bacterial penetration in these parts." It is the writer's opinion that these observations are of great importance in the application of any surgical procedure referable to the maxillary sinus. McDonald's findings based upon experimental study seem to prove that ciliary activity depends to a great degree upon a neurogenic control, and that any excess moisture modifies the extent and direction of ciliary propulsion. Assuming these observations to be true, it is evident that a fundamental principle in the treatment of this cavity would be the conservation of the cilia, regardless of their activity, by the most logical method based upon the surgical anatomy of the part involved. By so doing a physiological process is conserved and a surgical principle maintained. The virtue of the complete ablation of the mucous membrane and the clinical result must be defended against these facts.

The surgical anatomy of the maxillary antrum varies (8). Textbooks describe its embryology, configuration, and relation to surrounding structures. To correlate the applied anatomy relative to the surgery of this structure a series of maxillary bones were sectioned and observations made in reference to the comparative position of the most dependent part of the antral cavity, with that of the floor of the nasal fossa. Two sections, one through the anterior third and the second through

the posterior third of the inferior turbinate bone in the frontal plane, were made on a series of 64 superior maxillary bones. In 4 others, sagittal sections were made through the antrum so as to obtain a mental picture of the general appearance of the floor and for the purposes of illustration. A total of 68 maxillary antra were sectioned and observations made upon 196 specific sections. The results are presented not in reference to the sum total of sections but to the maxillary sinus floor as an entity and comparatively with the floor of the nasal fossa. The object sought was to determine in what percentage of antra drainage might be expected from the aspect of mechanical dependency. Other observations made in the respective antra were noted, principally for personal enlightenment, and, though not referable to the subject presented, have been briefly mentioned and reported.

A brief discussion of the nasal floor and the lateral nasal wall in reference to the maxillary antrum is necessary to clarify the findings. Anatomists describe the inferior turbinate as articulating with the inferior conchal crest on the medial surface of the body of the maxilla. Below the crest is a smooth concave surface belonging to the inferior meatus of the nose. The floor of the sinus descends below the level of the floor of the nasal cavity. From the floor of the antrum in the majority of cases septa of varying dimensions project upward and divide the cavity. The most frequent separates the premolar region in front from the third molar region behind, and may divide the sinus into two chambers (3, 9). Arthur Logan Turner, from a series of observations concludes that, in a maxillary sinus of average dimensions, the floor is on the plane of the floor of the nasal fossa. This statement raises the interesting





Fig. 3. Frontal section through both superior maxilla in the plane of the anterior one third of the inferior turbinate bones. It shows t 4 and A the maxillary sinuses and floor, B and B' the nasal floor, C and C' the inferior turbinate bones, D and D' the middle turbinate bones, E the nasal septum, F and F' the inferior nasal conchal crest. Notice the difference in the corresponding levels of the nasal floor with that of the maxillary sinus floor.



Fig. 4. Photograph of a section showing the floor of the maxillary sinus on the level with the floor of the nasal fossa. A the middle turbinate, B the ethmoid labyrinth, C the orbit and contents, note dark shadows of eye muscles, D the nasal floor, E the inferior turbinate bone, F the inferior conchal crest, F' the maxillary antrum and floor. Note that in this specimen the floor of the maxillary sinus is on the level of the floor of the nasal sinus, but also note the thickness of bone of the lower part of the conchal crest.



Fig. 5. Photograph of a section showing the floor of the maxillary sinus on the level with the floor of the nasal fossa. A the orbit and contents, B the maxillary floor and sinus cavity, C the posterior part of the frontal sinus extending over the orbit, D middle turbinate bone, E probe in external ostium of maxillary sinus, F the inferior turbinate bone, H the nasal sinus and floor, X the inferior conchal crest. Note the thickness of bone between the floor of the nasal fossa and the floor of the maxillary sinus.



Fig 5 Photograph of a section showing the floor of the maxillary sinus on the level with the floor of the nasal fossa. A the orbit and contents B the nasal septum C the superior turbinate bone D the middle turbinate bone E the inferior turbinate F the nasal floor H the floor of the maxillary sinus H' the inferior conchal crest. Note in this specimen as in Figures 3 and 4 the thickness of bone between the floor of the maxillary sinus and the nasal floor. Also notice dark areas in orbital contents representing internal rectus and inferior oblique muscle.

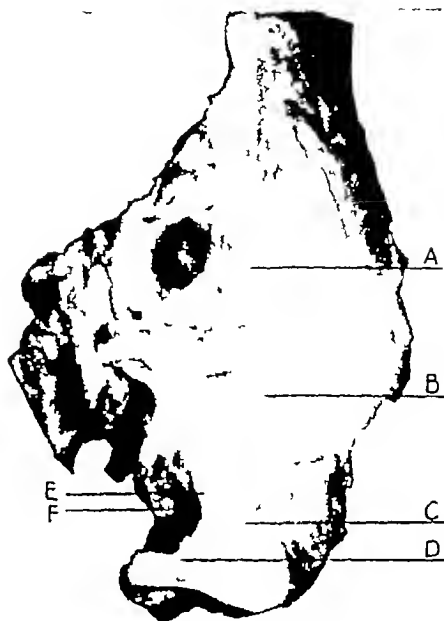


Fig 6 Photograph of section which shows the floor of the maxilla to be above the floor of the nasal fossa. A the orbit and contents B the maxillary sinus with its floor on the level of the inferior turbinate bone C the floor of the maxillary sinus D the nasal floor E the conchal crest. It demonstrates with what ease drainage may be obtained in such a case via the inferior meatus in contradistinction to that shown in the other photographs

problem of how often does a maxillary sinus of average dimensions occur, and in what percentage of antra does it, or does it not apply? Nevert reports certain phases of several hundred dissections from the Daniel Baugh Institute of Anatomy. He explains the presence of septa and abnormal ostia by stating that the embryology is an outpouching from the primitive ethmoidal infundibulum, and therefore we cannot expect to find the ostium maxillae to be of definite size and location. I have found this to be true.

In so far as the practical applicability of drainage into the nose from the maxillary sinus is concerned, it is the writer's opinion that the inferior conchal crest is the structure which serves as a barrier in attaining this end. This crest is compact bone, thick in its lower part, and rises above the nasal floor at times as much as 10 millimeters. It is doubtful whether it is possible in many cases to remove the crest to the level of the nasal floor without undue trauma. The use of

the Halle burr has been advocated (15). The writer has observed Halle's technique as he operated and has personally used it. There is no question but what one is able to remove more of the crest by this method. Whether the added trauma by the use of the burr compensates for the added drainage obtained must be questioned. The surgical anatomy presented does not warrant its use, other than in a limited number of cases. It possesses great merit in trimming roughened edges and completing a neat surgical procedure in the nasomaxillary approach as advocated independently by Canfield and Sturmann.

Of the 64 maxillary antra sectioned in a frontal plane, the following facts were determined in 19 it was clearly demonstrated that some part of the antral floor was below the most inferior plane of the nasal floor, in 21 the most dependent part was on the plane of the nasal floor, in 14 it was on the plane of the osseous conchal crest varying from the base to upper border, and in but 10 of the specimens was the floor of the maxillary sinus above the osseous conchal crest. In addition 17 of the antra were partially divided by septa, none

## TRIGEMINAL NEURALGIA

EXPERIENCES WITH AND TREATMENT EMPLOYED IN 468 PATIENTS DURING THE PAST 10 YEARS

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ALTHOUGH knowledge of the present day methods used for the alleviation of trigeminal neuralgia is widespread, there are, nevertheless, so many conflicting views relating to different aspects of treatment in the minds of both patients and physicians that it has seemed worth while to review our experiences in dealing with a fairly large group of individuals suffering from this malady and in so doing to relate what our policy has been in recommending various types of medical and surgical therapy.

It is still a frequent occurrence to have intelligent patients throw up their hands in horror when the so called radical operation of sensory root resection is proposed. Many of them say that they have been told, either by friends or physicians, that this operation should be under taken only "as a last resort," not only because they have heard that it was extremely dangerous, but because those who underwent this procedure were almost certain to be left with a "drooping face." It seems almost incredible that either or both of these highly overdrawn statements should persist today in view of their frequent refutation in medical literature by surgeons who have had the widest experience with trigeminal neuralgia. It cannot be denied that there is always some degree of danger in any surgical undertaking, but the mortality in operations for partial or total section of the sensory trigeminal root is, or should be, less than 1 per cent when the procedure is carried out by those who have been thoroughly trained in neurosurgery.

In regard to the facial palsy which is, apparently, so often associated in the lay mind with the radical operation, it must be said in all fairness that this does occasionally occur although its incidence is certainly not greater than 5 per cent. Furthermore, it is seldom complete and in the vast majority of patients clears up promptly and completely within 1 or 2 weeks. In rare instances it may take longer but in our own series there has not been a single case in which paralysis has been permanent.

In contrast to what has just been observed concerning division of the trigeminal root, one hears from perhaps an equal number of patients that alcohol injections are either of no value or that they are so painful they would rather have

their neuralgia than an injection. Again, in our opinion, these statements are not only greatly exaggerated but based upon faulty understanding. Alcohol injections, especially of the two lower divisions of the trigeminal nerve always give many months' relief from pain, *provided the nerve trunk has been exposed*. If they do not give such relief it means either one of two things, namely, that the nerve was not injected or the patient had some other type of neuralgia. As to the pain of giving an alcohol injection, the following, we think, is a fair statement. Most authorities believe that these injections should be given either without an anesthetic or after a preliminary injection of novocain around the nerve, because if the patient is under general anesthesia there can be no co-operation as to when the nerve is reached and the percentage of successful injections is consequently greatly lessened. This means that a certain amount of pain must be endured, but we have found that by using a small bore needle (22 gauge) there is in the great majority of cases only a prick when the needle pierces the skin, and subsequently a sharp but usually momentary radiating pain when the needle point enters the nerve. The latter is almost exactly like the pain which the patient has experienced frequently in the course of his neuralgia and is dissipated within a few moments by the immediate injection of alcohol which contains a little novocain.

From the foregoing observations it must be evident why no hard and fast rule can be laid down as to when injection or operation should be advocated. Indeed, there are some patients in whom the affliction is fortunately so mild that they may require no treatment at all or may perhaps be benefited by inhalations of trichloroethylene. We will return later to a fuller discussion of these subjects.

## DIFFERENTIAL DIAGNOSIS OF TRIGEMINAL NEURALGIA

In order to institute proper treatment for the condition in question, as in any other malady one must be certain that the patient has true trigeminal neuralgia and not one or another of the atypical neuralgias or pains in the facial region which at times may simulate the condition. Sev-

In addition to the patients seen and treated at the Lohrey Clinic since November 1922, this group represents all patients in the author's entire personal series at the Peter Bent Brigham Hospital since 1912. During the period mentioned in the literature, Dr. Harvey Cushing most kindly referred to the senior author for treatment, particularly in cases of trigeminal neuralgia, whether private or public, and paid cases. The name "graduated section" introduced by Dr. Cushing as well as an explanation of the term.

eral of these atypical neuralgias were described in detail by Cushing (1), in 1920. Although the diagnosis may be made almost at a glance when a typical paroxysm is observed, it is not always an easy matter, therefore, a few differential points concerning some of the commoner conditions causing confusion may be helpful.

Dental infections are common and small cavities with foreign objects, such as bristles of a tooth brush may cause pain which simulates a minor trigeminal neuralgia. Sinusitis can be ruled out by local tenderness and X-ray. Facial injuries usually have the history of trauma and are thus not readily mistaken, although one patient in the present series had a recurrence of pain for several weeks in his right lower jaw every time he ate or talked, 9 years subsequent to a total sensory root avulsion on the same side. Examination showed a complete anesthesia of the right trigeminal region and a definite localized tenderness over the angle of the right mandible. X-rays disclosed a fracture of the right lower jaw at the angle. There was no history of trauma with the exception of the fact that the patient had eaten some hardtack the night before the pain started. Transmission of pain in this instance must have been through sympathetic fibers.

Postherpetic neuralgia involving the trigeminal nerve usually clears up in several weeks in young individuals but in adults it may last for months or years with remissions. The pains are limited to the branches involved and are more or less continuous. However, they may come on spasmodically. The etiology of such a neuralgia is implied by the history, and examination usually shows the scars of herpetic vesicles together with hyperesthesia of the skin. The diagnosis is important because the pain is seldom if ever controlled by alcohol injection or even posterior root resection.

Sphenopalatine or Sluder's neuralgia caused by some infectious process of the sphenopalatine ganglion is probably relatively uncommon. The pains are usually at the base of the nose, around the upper jaw and eye, radiating backward to the ear and mastoid region, extending at times to the back of the neck, shoulder, and upper extremity. Neuralgias attributed to the geniculate ganglion involve the sensory portion of the seventh cranial nerve causing severe otalgia. The pain of glossopharyngeal neuralgia involves the tonsils, pharynx, and posterior part of the tongue. It is the same type of pain as trigeminal neuralgia, but differs in its distribution.

Sympathetic pains are usually described as dull, aching, burning, or pressure pains varying in in-

tensity. They seldom follow any anatomical distribution of nerves. The orbit, cheek, and temporal region are usually involved. The pains usually last several hours, and may persist intermittently for months. The intensity usually varies with the nervous stress of the patient. Associated symptoms such as flushing of the face, increased lacrimation, and salivation are common.

Tumors involving the gasserian ganglion produce severe and usually persistent pain while examination reveals the relative hypesthesia and later a sensory and motor paralysis. High cervical spinal cord tumors have been alleged to cause severe pain in the trigeminal region, but in these cases there are other associated signs and symptoms, making the diagnosis possible if a careful general neurological examination is made.

#### SYMPTOMATOLOGY

The subjective symptoms of trigeminal neuralgia are usually so graphic that the diagnosis is unmistakable. A frequent story is that the patient was seized with a sudden pain in one side of the face "like a bolt of lightning," lasting for several moments, leaving as suddenly as it came, with no residual aches or pains and reappearing at frequent intervals. The character of the pains are detailed by different adjectives depending on the descriptive powers of the patient and the severity of the attacks, but all with the same meaning. The pains come on in paroxysms of rapid, successive stabs confined to the limits of the branch or branches involved. Some authors state that pains should always radiate to the very end of the branches at the median line. In our patients, when paroxysms were severe, pain has extended to the peripheral limits of the nerve but in milder attacks this has not been the rule. Too much emphasis cannot be laid upon the fact that there is practically always entire freedom from pain or discomfort between attacks. There are frequently periods of remission during which time the patient is wholly relieved, or is fairly comfortable for a matter of several days, months, or even years. During a severe bout of pain, the paroxysms vary in frequency, coming on every few minutes or only a few times daily. A region of increased irritability commonly called the "trigger zone" is often present and when stimulated by washing the face, shaving, chewing, talking, or smiling, a spasm is induced thus explaining the masklike expression of the affected side of the face, also the accumulation of dirt as well as the peculiar headgear some patients use as a prophylactic. Other objective signs than those mentioned vary with the individual. Patients with a

highly nervous makeup may demonstrate their agony during an attack by throwing themselves on the floor screaming and rubbing the face on the affected side. Others more stoical may merely rub their cheek or make a few chewing movements, stopping any conversation they are engaged in until the pain has left, and then resume their conversation.

#### ETIOLOGY

The cause of trigeminal neuralgia is unknown. The most plausible theory would seem to be that of Sir Willfred Harris (6) who believes that dental infections are in all probability the underlying factor although it is well recognized that once the neuralgia has started, removal of infected teeth has no influence upon it. Dandy feels that external pressure upon the sensory root by tumors or blood vessels may at times be the cause of the *douloureux*. Multiple sclerosis has also been given as a possible etiological factor but only 3 cases of this malady have been found in our series. Trigeminal neuralgia occurs most frequently in patients of middle or advanced age. In our group, 60 per cent occurred between the ages of 50 and 70 years and over 90 per cent in patients between 40 to 80 years of age. The youngest patient was 16 and the oldest 93 when they came for treatment.

TABLE I—AGE INCIDENCE

Age in years	Cases
0-20	
20-30	
30-40	29
40-50	14
50-60	27
60-70	60
70-80	9
80-90	
90-100	

Women were affected much more frequently than men in our series in the ratio of almost exactly 60 to 40 per cent. Fifty per cent occurred on the right side, 45.3 per cent on the left, and 4.1 per cent were bilateral.

TABLE II—SEX INCIDENCE AND SIDE AFFECTED

	Cases	Per cent
Males	186	40.8
Females	23	50
Right side	37	5.7
Left side	90.3	44
Bilateral	9	4

The division involved alone most frequently was the third, which occurred in 42 per cent of all cases the second division in 24 per cent the

second and third together in 21.9 per cent the first and second together in 3.8 per cent (Table III)

TABLE III—FREQUENCY OF DIVISIONS INVOLVED

Division of trigeminal	Per cent
1st division	9
2d division	24
3d division	42
1st, 2d, 3d divisions	4.7
2d, 3d divisions	9
1st, 3d divisions	3.8

#### TREATMENT

We feel that to the present day there is no ideally perfect treatment for trigeminal neuralgia because although permanent relief of pain can be promised the patient there are certain discomforts associated with the numbness which must be substituted for this. In explanation of such a statement, however it must be said at once that certainly 90 per cent of all persons who are now treated by modern methods would consider the treatment as most satisfactory and not regard the discomfort from numbness or paresthesias as any particular hardship. Even during the past decade, many things have been learned which make the treatment more comfortable and lessen the possibility of operative or postoperative complications. Preserving the motor root (5) and conservation of the ophthalmic fibers (4) in the lower division neuralgias are striking examples directed toward this end. Furthermore, the total or differential injection of the ganglion as practiced by Harris (7) has great possibilities in skilled hands. Finally the operation advocated by Dandy in which the nerve root is partially divided at the point, has apparently reduced the resultant numbness to a very great extent, but we believe that this procedure is at least potentially more dangerous than the accepted temporal route.

The treatment of trigeminal neuralgia may be divided into the conservative and radical, the conservative consisting in non-operative and minor operative procedures, the radical in root ablation. As already intimated, in order to obtain permanent relief one must exchange pain for a permanent numbness of the part involved. Such an exchange is accepted cheerfully by the majority of patients who grasp at anything which will end the excruciating pain. However it must be emphasized that a few mind the numbness and paresthesia following ablation more than the previous pain and it is because of this small group that one hesitates to advise the radical operation before acquainting them thoroughly with the numbness by less radical measures.

Therefore, as with any other disease, the treatment must be suited to the patient and not the patient to the treatment.

We do not advocate any single procedure, but wish to describe our own method of dealing with individuals having trigeminal neuralgia. Patients usually consult a neurosurgeon after every possible medical treatment has been tried. The teeth, as a rule, have been removed on the side affected, although in recent years this has been less frequent since dentists recognize the malady and advise against this practice, if the X-ray shows no pathological condition. Narcotics are frequently taken, but fortunately do little to relieve the pain, thus preventing drug addiction. When the patient does come he is interested usually in getting rid of the pain immediately.

*Treatment with trichlorethylene* If there is no question as to the diagnosis and the attack is mild, inhalations of trichlorethylene are advised with definite instructions that 20 to 30 drops be placed on a handkerchief or piece of cloth and held closely to the nose. The fumes are to be inhaled until no odor is detected, a matter of a few minutes. This is to be done three times a day for two weeks, regardless of whether the pains are present or not, provided pain is not so intense that the patient should be in a recumbent position on one side or the other so that if they should become partly anesthetized, the hand will drop away from the nose, stopping the inhalation.

Ninety patients were given treatment with trichlorethylene and have been followed carefully. In this group, nearly one-half obtained sufficient relief so that they did not feel it necessary to have any other form of treatment for their neuralgia for periods of 6 months up to 6 years. The remaining patients obtained no relief or it was so slight that something more radical was indicated within a short space of time.

*Alcohol injections* If no relief is obtained from trichlorethylene, the patient is then asked to come in for alcohol injection of the peripheral nerve trunk. At no time is avulsion of the root advised without first giving at least one such injection. This policy is followed for two reasons. In the first place, it makes the patient acquainted with the numbness which must follow any surgical procedure upon the trigeminal system. This may seem to be a small matter, but experience has shown that some patients are greatly annoyed by such an anesthesia and the various sensations which accompany it. These sensations are described as "burning," "twisting," or "like wires in my face," and occasionally are complained of as much as or even more than the original pain.

When an alcohol injection only has been performed, normal sensation returns to the area injected and later, when there is a recurrence of the neuralgia the patient is much more likely to be satisfied with treatment, realizing that after all, the discomfort from these paresthesias is not to be compared with the agonizing neuralgia pain. A second reason for preceding root section by an injection is to make sure, in the occasional instances in which the diagnosis may be uncertain, that the patient has true trigeminal neuralgia, since it is now well known that division of the sensory root of the trigeminal will not relieve the atypical facial pains which simulate tic douloureux. Both of these points as well as others were emphasized by Cushing (2) in 1920.

An alcohol injection can be performed quickly in the office with immediate relief of the pain in all cases, if a fair hit of the nerve has been made. At times, if two divisions are involved, mainly the second and the third, each is injected at the same session. Usually, however, the affliction has started in one branch only but pain may "overflow" into the area adjacent. In such cases, if an injection is made into the nerve primarily affected, this "overflow" is practically always controlled.

Before alcohol injections are attempted, one must have a thorough knowledge of the skull with relation to the structures around the exits of the nerve trunks. This can be obtained only by dissection of the head and neck, as well as by injecting the nerve trunks in cadavers with colored solutions, in this way becoming familiar with the bony landmarks and approximate depth of the foramina rotundum and ovale. After one has become acquainted with these landmarks on the cadaver, it is important, if possible, to see injections performed by someone who has had experience with the procedure and likewise to do injections on patients under supervision. A most important faculty to develop is that of being able to visualize deep structures in three dimensions.

For the actual injection a small instrument set is all that is necessary. This consists in a 5 cubic centimeter Luer-Lok syringe, two No. 22 gauge needles 3 inches long, a fine short needle for supra-orbital and infra-orbital injections, a centimeter measure, a hemostat, a prepared solution of 80 per cent alcohol containing 1 per cent of novocain, and a little bone wax to use as a marker on the needle. For all injections the patient is asked to lie flat on the back on a table of sufficient height for the operator to be in an easy position. For deep injections of the second and third divisions, the patient's head is turned well over to the oppo-



Fig. 1. Front view to show approximate up and angle of needle for third division injection.



Fig. 2. Posterior view showing relation of needle to auditory meatus in third division injection.

site side and rests on a sand bag about 1 to 3 inches in thickness. No premedication is given unless patients are unusually apprehensive and nervous. The reason for this is that the ultimate success of the injection depends on their co-operation.

It is not necessary for the operator to clean up or to use rubber gloves for giving injections in the manner to which we have become accustomed. Our preparatory routine is as follows. The sterile injection set is opened and with the sterile hemostat contained in the set an appropriate needle is adjusted to the syringe. If an injection of the foramen ovale or rotundum is contemplated, a bit of bone wax is pinched around the needle, 1 centimeter beyond the usual depth at which these structures are reached. Two cubic centimeters of the 80 per cent alcohol mixture is drawn into the syringe after which the appropriate area on the patient's cheek is sterilized with 70 per cent alcohol. A small piece of gauze dampened with alcohol is placed over the area to be injected in order that landmarks may be palpated through this. The approaches which we use to the foramen ovale and foramen rotundum are essentially the same as those described by Hartel and Harris.

**Third division injection.** For this procedure the bone wax marker should be placed on the needle at a distance of 5.5 centimeters from the point, thus giving 1 centimeter less  $y$  between this marker and the depth at which the nerve should be reached. The syringe with attached needle is taken in one hand, while the index finger of the other palpates through the sterile gauze the highest point of the notch in the lower border of the

zygomatic process. The patient is then instructed concerning the procedure by being told that there will first be a slight prick as the skin is pierced, after which no great discomfort will be felt until the nerve is entered, when there should be experienced a pain similar to the neuralgic pain which ordinarily radiates down the lower jaw to the chin or to the front of the tongue. Patients are told particularly to let the operator know if pain radiates upward into the temple or backward toward the ear because when radiation occurs in these directions it means that the needle has impinged upon the meningeal artery or the eustachian tube respectively.

The sterile gauze is now removed from the cheek and the needle inserted just below the zygomatic notch at the point where a slight imprint will have been left by the palpating finger pressed upon the gauze. The needle is directed slightly upward and backward and at a depth of 4.5 centimeters, the nerve trunk may be reached upon the first attempt (Figs. 1 and 2). If pain radiates correctly a drop or two of alcohol is injected. This causes a momentary severe pain over the course of the nerve, but is followed immediately by numbness and cessation of pain. If the nerve is not reached at the usual depth, our practice is to withdraw the needle 1 centimeter or two and then direct it somewhat forward so as

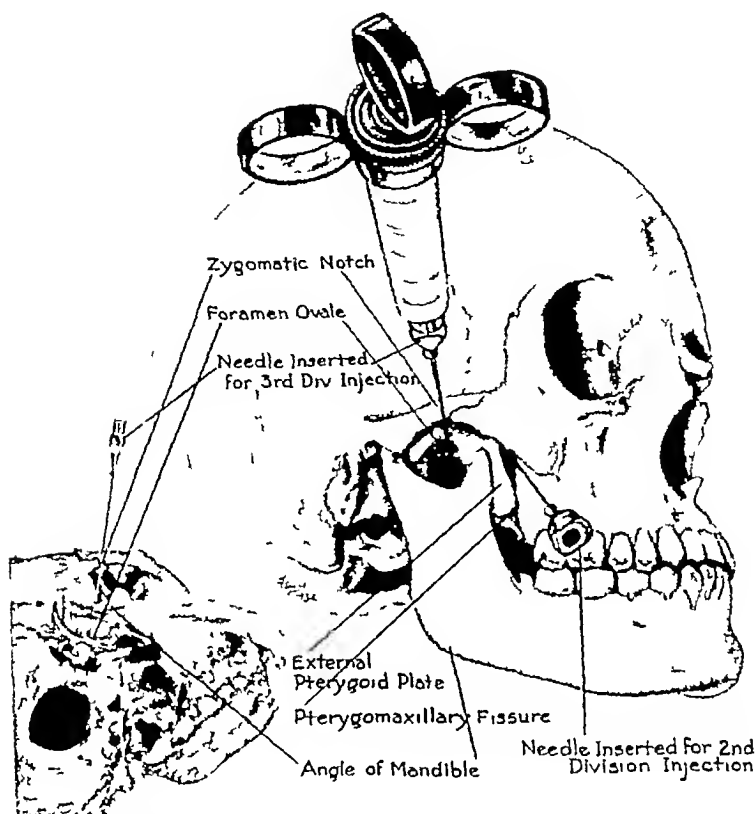


Fig 3 Two views of skull to show various landmarks and relationships with needles inserted for second and third division injections

to come down upon the external pterygoid plate. This is an essential landmark because the foramen ovale lies just posterior and slightly medial to it (Fig 3). With this orientation the needle is again withdrawn somewhat and directed a little backward until the nerve is entered as evidenced by pain radiation. It may be necessary to repeat this process several times, and also it must be remembered that there are slight variations as to the depth at which the foramen lies. In some individuals it may be reached at slightly less than 4.5 centimeters, and rarely at a depth as great as 5 centimeters from the skin.

When the nerve trunk has been entered and a few drops of alcohol injected, the patient's lower lip near the median line is tested for anesthesia. This should be done with a pinpoint and the patient's eyes should be closed. If a fair hit has been made, the sensory loss is almost immediate on this portion of the lip, the lower gum, and half of the anterior two-thirds of the tongue. Having

determined this, we then inject about 1 cubic centimeter of alcohol very slowly, often pushing the needle gently inward for a millimeter or two during the process in order to be sure that the substance of the nerve is wholly injected. The needle is then withdrawn and pressure made over its point of entrance with sterile gauze in order to prevent oozing. The patient is now asked to open the mouth. If injection of the third division has been complete, the lower jaw will deviate distinctly toward the affected side.

One further point regarding the injection should be noted. At times when the needle is in the proper position and depth, there is no radiation of pain down the jaw but severe pain is present at the tip of the needle. This happens in a fairly large percentage of cases. A drop of alcohol may then be injected and it usually brings on the radiation of pain followed by numbness, indicating that a fair hit has been made. The reason care should be taken in injecting only very small





Fig. 4. Front view of patient showing approximate position and angle of needle for second division injection from anterior approach.

amounts slowly is that at times the point of the needle enters the foramen ovale unwittingly. If the point happens to be in the subarachnoid space around the ganglion and alcohol is injected, severe reactions as well as permanent damage may be done. If, on the other hand, only a drop has been injected and the patient develops nystagmus, vomiting, or other untoward symptoms, the needle should be withdrawn. The resistance with which the alcohol enters is usually a reliable indicator as to whether the needle is in nerve tissue provided, of course, that the position and depth are proper, as well as the definite reduction of pain. Should the patient complain of severe pain in the ear as the injection is started, it may mean the alcohol is entering the eustachian tube or has struck a small branch from the trigeminal which innervates the ear. Reference to Table IV shows that of 600 alcohol injections, 345 or somewhat over half, were given to the third division.

TABLE IV.—NUMBER AND TYPE OF INJECTIONS

Type	No.	Per cent
3d division	345	57.5
2d division	98	16.3
Infraorbital	147	24.4
Supraorbital		8
Ganglion		8

The average period of relief from third division injections was 4.3 months, the shortest period being 9 months and the longest 8 years (cf Table V).

TABLE V.—AVERAGE RELIEF FROM INJECTIONS WITH ALCOHOL

Division	Months
Supraorbital	6
Infraorbital	4
Maxillary	4
Mandibular	14.3

*Second division injection.* Trigeminal neuralgia involved the superior maxillary branch in 24.3 per cent of our cases. Pain may be controlled either by a deep injection at the foramen rotundum or at the infraorbital foramen depending entirely upon its distribution. The infraorbital injection is usually sufficient if the roof of the mouth is not involved. Since this foramen is more accessible than the rotundum, such an injection is relatively simple and, therefore, more frequently chosen.

In doing the deep injection at the foramen rotundum, it is our custom to use only two of the described routes, the anterior approach, so called because the needle enters the pterygomaxillary fissure anterior to the coronoid process of the mandible while posteriorly to the coronoid is the posterior approach. The anterior approach is more direct and usually more successful. However at times, it is impossible to reach the pterygomaxillary fissure because of the overhanging edge of the maxilla, and in such patients the posterior approach may be easier.

The same preliminary procedures as in the third division injection are used for the deep second and infraorbital procedures, in that the patients are given no preliminary medication and the skin is sterilized with 70 per cent alcohol. In the anterior approach, the needle is pressed through the skin just beneath the anterior portion of the zygoma and anterior to the coronoid process, as shown in Figure 4. The needle passes medially at a 40 degree angle, anterior to the coronoid process, and immediately posterior to the maxillary process. As it enters the pterygomaxillary fissure, which is a narrow opening about 0.5 centimeter wide, it usually strikes the external pterygoid plate behind or the posterior border of the maxilla in front. The nerve, as a rule, is reached at 5.5 centimeters depending of course, on the width of the face of the patient (see Fig. 3). It is important that one should not go deeper than 6 centimeters at any time, because

if possible injury to important structures, especially the optic nerve. If the external pterygoid plate is struck, it can be used as a valuable landmark, the foramen rotundum lying anterior and 0.75 to 1 centimeter deeper. If the posterior portion of the maxilla is reached before entering

the pterygomaxillary fissure, it will also serve as a guide, keeping in mind that the fissure in which the nerve lies is bounded by the maxilla anteriorly and the external pterygoid plate posteriorly. By gentle manipulation of the needle, the nerve will be reached, if no unusual bony prominences make it impossible. Throughout the procedure, one should have a mental picture of the deep structures. As soon as the needle enters the nerve tissue, a spray of pain will be felt along the course of the nerve. Here, again, only a few drops of alcohol are injected at a time, if complete anesthesia of the upper lip, ala of the nose, and roof of the mouth is obtained, 1 or 2 cubic centimeters more is then injected slowly. The most reliable place to test the anesthesia obtained is on the upper lip and the ala of the nose, while the patient has the eyes closed.

When the roof of the mouth and gum is not involved, the infraorbital nerve is injected as it comes out of its foramen. This is relatively simple because of its position. It is located approximately 0.8 centimeter beneath the inferior orbital rim and 2.5 centimeters from the midline. Instead of having the face turned to one side, it is easier to have the face straight up. The index finger of the left hand is placed firmly over the inferior orbital ridge so as to avoid injuring the eyeball and surrounding tissue by having the needle slip over the bony rim. The point of the needle is then inserted into the nasolabial fold about 2.5 centimeters from the midline, directing it at a very acute angle toward the infraorbital foramen. As a rule one has no difficulty in telling when the tip of the needle enters the foramen. As it does so, the patient immediately complains of a spray of pain radiating to the ala of the nose, cheek, and upper lip. The alcohol is then injected, a few drops at a time, anesthesia usually resulting immediately. Frequently, however, the infraorbital nerve branches before it leaves the canal, thus making it necessary to probe gently until the tip of the needle enters. As it does so, the patient immediately complains of a spray of pain radiating to the ala of the nose, cheek, and upper lip. The alcohol is then injected, a few drops at a time, anesthesia usually resulting immediately. Frequently, however, the infraorbital nerve branches before it leaves the canal, thus making it necessary to probe gently with the tip of the needle and to inject a few drops each time the patient has a twinge of pain. During the procedure, it is a good policy to keep firm digital pressure in the immediate vicinity of the needle, preventing hematoma formation because injury to the infraorbital artery is at times unavoidable.

Such pressure also prevents the backing up of alcohol in the superficial subcutaneous tissue. This is important as alcohol in this region may cause a drooping of the upper lip due to injury of the facial branches. In some individuals the bone covering the maxillary sinus is of paper thickness, thus allowing the point of the needle to enter the sinus with the least pressure. This happened once in this clinic without harmful results and probably would have been overlooked if bloody alcohol had not escaped from the nostril on the side of the injection as the patient stooped over to pick something up from the floor immediately following the injection. There have been 150 second division injections in our series, the average period of relief being 12.4 months, ranging from 6 months to 3 years (Table V).

The first division can be injected at the notch in the supraorbital ridge. The results are not as satisfactory as supraorbital neurectomy because the supraorbital nerves usually fan out over the supraorbital ridge, making it difficult to strike all the fibers with alcohol. Only twelve supraorbital injections were performed, the average relief from these being 6 months.

There have been occasional slight complications of alcohol injections such as hematomas, temporary dizziness, and headaches, and in one instance transient nystagmus and diplopia. Two patients had sixth nerve palsies lasting for an hour or two and one patient had temporary dilatation of the pupils after a third division injection. Only one patient was advised to enter the hospital and that was because of dizziness, nystagmus, headache, and diplopia following a third division injection in which the tip of the needle must unwittingly have entered the subarachnoid space surrounding the ganglion. The reason for this assumption is that the entire half of her face became anesthetic, lasting one hour. The patient was entirely well the next morning and had no ill effects.

The real objection to alcohol injections is that they give only temporary relief. The patient realizes that the pain will return sooner or later and is, therefore, more or less apprehensive of this fact. The other objections are that they are painful and in certain individuals the nerves cannot be reached properly because of scar formation from previous injections or because of abnormal bony protuberances, especially in the region of the foramen rotundum.

There are no contra-indications to alcohol injections with the exception of local infections in the skin or tissues through which the needle must pass.

*Ganglion injections.* In regard to injection of the gasserian ganglion itself we feel that unless one has become especially proficient with this delicate procedure, it is probably more hazardous than the usual sensory root avulsion when the latter is carried out by a properly qualified surgeon. Relatively few attempts have been made to inject the ganglion in this clinic, the total number being twelve. They were done either because the patient refused operation or was physically unfit for operation.

Peripheral neurectomies are performed only when pains are limited to the supraorbital division. Two to four years' relief is obtained in this way. The procedure is very simple and may be repeated several times. The great advantage of this operation is that it avoids the dangers of keratitis that may follow a complete sensory root avulsion.

*Sensory root operation.* A rigid rule is followed in that no patients are operated on for section of the sensory root without making them thoroughly acquainted with the numbness of the face which will inevitably follow. This is done by giving at least one alcohol injection. The numbness itself is uncomfortable and the feeling cannot be appreciated by even the most intelligent patients until they have actually experienced it. When they have been made to realize that numbness of the face is infinitely better than the previous pain or if injections become too difficult because of scar tissue the radical operation is advised. The treatment of trigeminal neuralgia is one of election and therefore, if good results are obtained by alcohol injections which are entirely without danger in the hands of the experienced, there seems to be no particular reason for demanding that the patient have a sensory root avulsion. Several things, however, must be kept in mind and these are that, if the patient is young and has a severe major neuralgia, it is hardly fair to ask him to go through years of more or less painful alcohol injections. The knowledge that the pain is bound to recur and the necessity of resorting to an injection each time this happens, is by no means conducive to maintaining the proper frame of mind to compete in every day business. On the

other hand, in many patients beyond the age of 70 years, a single injection may see them comfortably through their allotted span of life without resorting to a more radical procedure.

The technique used in the sensory root avulsion will not be described here as it is the same as that used by practically all neurosurgeons and several well illustrated articles have been written on this subject. The operation has been performed on 176 patients during the past 10 years without a fatality. In all instances, the temporal route was employed. The complications were minor with the exception of the rare development of keratitis in approximately 5 per cent of those in whom complete root avulsion was practiced while perhaps another 5 per cent considered the subsequent paresthesia almost as bad as the original pain. Naturally it is these patients that make the neurosurgeon hesitate in advising the radical operation without previously acquainting them with the numbness by alcohol injection. However the great majority of patients are most appreciative and grateful, making the operation one of the most satisfactory that a surgeon can perform. A temporary facial palsy occurred in 6 patients during the earlier years, but this complication has not been noted during the past 5 year period. Whenever the first division has been included in the root resection, the most meticulous post-operative care of the eye cannot be too greatly emphasized. The patients on their discharge from the hospital are instructed to wear specially made glasses to serve to keep the cornea free from trauma and are given written directions as to the care of the eye if any suspicion of inflammation arises.

#### BIBLIOGRAPHY

1. CUSHING, HARVEY. *Am J M Sc* 1920, 160 57
2. *Idem*. *J Am M Ass*, 1920, 73 44-443
3. DANDY, WALTER E. *Arch Surg* 1920, 8 687-734
4. FRAZER, C H. *Arch Neurol & Psychiat* 1926, 87 730
5. *Idem*. *Arch Neurol & Psychiat* 1925, 3 376
6. HARRIS, WILFRED. *Neuritis and Neuralgia*. London 1920
7. *Idem*. *Brit M J* 1912, July 28
8. HARTZ, F. *Deutsche Zeitsch f Chir* 1914, 86 499-55

END-RESULTS WITH THE WATKINS' INTERPOSITION OPERATION<sup>1</sup>

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THE treatment of uterine prolapse and cystocele in women past the menopause perhaps seems an old and time worn subject, for it is nearly 35 years since Watkins first described the method which we largely use for the treatment of such cases. A review of the recent literature and transactions of societies, however, reveals that gynecologists are still divided between more or less ardent advocates of this method and those who oppose it. Many of the opponents prefer the Mayo type of vaginal hysterectomy and some still use a combination of vaginal plastic repair with abdominal suspension of the uterus. No less than four articles upon various phases of this subject have appeared in a single journal<sup>2</sup> within a recent 6 months' period, ample evidence that the subject is still one of active current interest. In one of these articles Robert T. Frank states that he uses the interposition operation only occasionally in cases with large buliard ball cystocele and without marked prolapse. His most frequent procedure has been plastic vaginal repair and ventrofixation, but he reports only 66 per cent satisfactory results in a series of 414 cases. In the discussion of a report of "Two Cases of Pregnancy Following the Watkins Interposition Operation" by Dr. Carl H. Ill, of Newark, before the New York Obstetrical Society recently, Dr. B. P. Watson unreservedly condemned the procedure in the following words: "I believe that all of these complications could have been avoided had interposition not been done. I regard it as a bad operation." On the other hand, Coventry and Moe have reported 69 perfect anatomical results in 70 operations and in 66 all symptoms were entirely relieved. Laws, of Philadelphia, reported one failure in 33 operations.

We have found the interposition operation when used in properly selected patients a most satisfactory procedure. Dr. Thomas S. Cullen has been one of its most ardent advocates for years, and under his championship it has become very popular among most of the members of the department, though we do have one or two rather ardent advocates of the vaginal hysterectomy.

We restrict the use of the interposition to patients near, at, or past, the menopause, except in an occasional case where future childbearing is strongly contra-indicated. In such cases, of course a careful tubal sterilization is done at the time of

operation. Following this rule we have had no cases of pregnancy in the past 18 years. Contrary to Ward, we do not find that the degree of prolapse matters and use the operation for complete procidentia as well as lesser degrees of prolapse.

Most of the members of the department restrict the use of the vaginal hysterectomy to those cases in which some uterine pathology makes hysterectomy advisable. In the younger women we use a combination of the necessary vaginal repair with abdominal suspension of the uterus, the Mayo modification of the Gilliam technique being used.

In the preparation of this paper I have studied the ultimate results of the interposition operations done during the years 1927-1931 inclusive, and also, for sake of comparison, the results in the much smaller series of vaginal hysterectomies done during the same period. There were 68 of the former and 26 of the latter operations done during this time. I have been able to obtain recent follow-up information on 48 of the patients who underwent interposition operations and on 17 of those who had vaginal hysterectomies.

Of the 68 patients who had interposition operations, all but 9 were 45 years old or older, and all but 9 were at or past the menopause. The oldest patient was 78, the youngest 26. Two patients were over 70 and two under 30.

Sixty of the patients were white and eight colored. We have noticed over a period of years in a clinic treating a large number of colored patients the relative rarity of conditions requiring vaginal plastic work in this race.

There was one nulliparous patient in the series and one in whom the number of children was not recorded. The average number of term deliveries was 4.3. Four patients had had ten or more children.

The symptoms of which the patients complained were the usual ones in such a group: backache, dragging sensation in the pelvis, dysuria, frequency, constipation and evidence of prolapse.

The extent of the various anatomical defects in the 68 patients is shown in the accompanying tables.

In addition to the interposition operation, the cervix was amputated in 48 patients. In all except 3 cases a perineorrhaphy and posterior colporrhaphy were done. In these 3 cases the perineal relaxation and rectocele were so slight as not to

<sup>1</sup>Am. J. Obst. & Gynec.

<sup>2</sup>From the Department of Gynecology of the Johns Hopkins University and Hospital. Paper presented before the Bay Ridge Medical Society, Brooklyn, New York, May 9, 1933.

TABLE I—DEGREE OF PROLAPSE

Degree of prolapse	No. of patients
None (large cystocele)	4
First degree	8
Second degree	45
Complete procidentia	5

TABLE II—SIZE OF CYSTOCELE

Size of Cystocele	No. of patients
Small	5
Moderate	
Large	54

TABLE III—SIZE OF RECTOCELE

Size of Rectocele	No. of patients
None	
Small	6
Moderate	
Large	29

require repair. Tubal sterilization was considered advisable and was carried out in 6 patients.

The operations were performed by 11 different operators. Thirty-five of them were done by 5 different members of the visiting staff and the 33 remaining by the various residents and assistant residents during the period under consideration. This fact disposes of any criticism or objection that might be offered that the operation is one capable of being performed only by operators of long experience and superior skill, for while the residents and assistant residents in our department are all men with 4 to 5 years of thorough postgraduate training in pathology, anatomy and surgical technique, they are still serving an apprenticeship in gynecological surgery.

#### RESULTS

One of the 68 patients died of pulmonary embolus during postoperative convalescence. The 67 others were discharged as well, so far as their gynecological conditions were concerned, after an average convalescence of 22 days. This perhaps may impress some as a rather prolonged period of postoperative convalescence, but our attitude in the treatment of such cases is that we are dealing essentially with a hernia, and that one of the most important factors in treatment is to relieve the repaired structures of all possible strain until ample time has elapsed for thorough healing. We therefore make it a practice to keep such patients in bed for fully 2 weeks following the operation and then permit them to get up and about very gradually over a period of several days.

Of the 67 patients discharged, we have been able to obtain recent data on the ultimate result in 48. Of these all but 2 had excellent anatomical

TABLE IV—AMOUNT OF PERINEAL RITLACATION

Ritlacation	No. of patients
Slight	
Moderate	
Marked	43
Third degree laceration	5

TABLE V—WATKINS INTERPOSITION OPERATION AND VAGINAL HYSTERECTOMY—END-RESULTS

	Interposition		Vaginal hysterectomy	
	Number of patients	Per cent	Number of patients	Per cent
Number of operations	66		26	
Number followed	28		17	
Perfect results	20	66.6		27
Satisfactory results	11	39		
Unsatisfactory results				29

results. In 2 after 5 years of complete relief, there was recurrence of moderate prolapsus. In both of these the original prolapsus was of the second degree. None of the 10 patients followed who were originally suffering from complete procidentia has had a recurrence. In 4 patients with perfect symptomatic results and perfect cure of cystocele and prolapsus, it was found on examination that there was still slight rectocele above the perineum. In these the posterior repair was probably not carried sufficiently high to reduce the rectocele completely but as the patients were entirely free from symptoms the results may be considered satisfactory. Three patients complained of dyspareunia. In all of these the result of the interposition was perfect, but a too extensive perineal rhyphid had resulted in a rather small introitus. Nine patients still complained of some frequency and dysuria. In 6 of these the symptoms were due to the presence of a urethral caruncle which has been removed by fulguration with subsequent relief. The others had all had considerable frequency and dysuria before operation and the symptoms, though still present, have been much less annoying since. Four of them had definite urinary infections for which they received treatments. In summary then we may say that 2 cases may be considered unsatisfactory because of recurrence after 5 years. In 32 the results have been perfect anatomically and symptomatically. In 14 the results have been satisfactory but cannot be considered perfect because of slight residual symptoms or slight anatomical defects not really associated with the interposition.

In 92 Shaw reported the results of the same operation for the same clinic up to that time. He

was able to obtain data on only 58 of 118 patients. Of these 21 had been operated upon since 1915 and among these 21 there was 1 failure. Among those patients operated upon prior to 1915, he found 12 failures, but it is quite evident from his report that in the earlier years the careful selection of patients as regards age, etc., now practiced was not adhered to. For instance, 34 of his patients were under 40 years of age.

Brady, in 1925, reported a series of 48 followed patients operated upon by Dr. Thomas S. Cullen. In 47 of these the result was entirely satisfactory while in one there appeared after 10 years a recurrent prolapse of the anterior vaginal wall. This was repaired with excellent result.

If now we add Shaw's 21 patients since 1915, Brady's 48, and the present series of 48, we have a total of 117 properly selected patients treated by this method in whom evidence of recurrence could be found in only 4, or approximately 3.5 per cent. In my smaller series the 2 failures give a percentage of slightly more than 4 per cent.

Now let us consider for a moment the smaller series of 26 vaginal hysterectomies done during the years 1927 to 1931 inclusive. These 26 operations were done by 9 different operators, 14 of them were done by 4 members of the visiting staff, and the 12 remaining by the 5 residents during this period. Equal care was exercised in the selection of these patients for operation as in the preceding group. The patients with one exception were all near or past the menopause. This one was 34 years of age and in addition to descensus and a large cystocele had been suffering from persistent menorrhagia for 2 years. The oldest patient in the series was 70, the average age was exactly 50. In 13 of the patients the operation was chosen in preference to an interposition because of some uterine pathology requiring removal of the uterus, and in the 13 remaining it was the operator's preference.

In 11 of the patients the prolapse was of first degree, in 7 of the second degree, and in 8 there was complete procidentia. The 26 patients were all discharged as well after an average convalescence of 25 days. This increased average of convalescence is due to three patients whose convalescence was greatly prolonged by complications. One of these had bronchopneumonia, another had bilateral thrombophlebitis, and the third developed a rectovaginal fistula, which was later successfully closed.

We have been able to obtain recent data on 17 of the 26 patients. In 12 the anatomical result

was good, while 3 showed recurrent cystocele, and 2 others prolapse of the vaginal vault. In one of the latter there was also a large enterocele. Of the 12 with good anatomical result, 4 complained of urinary symptoms.

We have then practically 30 per cent of anatomical failures with vaginal hysterectomy as opposed to approximately 4 per cent anatomical failures with the interposition operation. The criticism cannot be offered that the failures with the vaginal hysterectomy were due to inexperience of the operators, for 2 patients in whom failures occurred were operated upon by the same operator and 2 others by another. Both of these men are surgeons who have had long experience and have superior skill and one of them is probably the most ardent advocate of the procedure to be found in the department.

In summary, then, I believe I am justified in saying that in our experience the Watkins' interposition operation is the procedure of choice for the treatment of prolapse of the uterus in women past the menopause. It is preferable to a combination of vaginal plastic with abdominal suspension because it is a shorter and simpler procedure and avoids the increased risks incident to laparotomy. The combined operation, however, is the procedure of choice in women during the child-bearing period. The interposition is preferable to the vaginal hysterectomy because, in our experience at least, it gives better permanent results, it is easier to perform, and, in cases in which there happens to be a recurrence, a second repair is much simpler with the uterus still present. We can find no reason for considering an advanced degree of prolapse a contra-indication for interposition, for in all cases with complete procidentia whom we have been able to follow the results were perfect. We believe that vaginal hysterectomy finds its chief use in cases in which a repair is necessary for the cure of cystocele and prolapse, and the removal of the uterus is at the same time indicated.

#### BIBLIOGRAPHY

1. BRADY, LEO. *Surg., Gynec. & Obst.*, 1926, 43, 476.
2. COVENTRY, W. A., and MOE, RUSSELL. *J. Am. J. Obst. & Gynec.*, 1933, 25, 257.
3. FRANK, ROBERT T. *Am. J. Obst. & Gynec.*, 1932, 24, 574.
4. LAWS, GEORGE M. *Am. J. Obst. & Gynec.*, 1932, 24, 864.
5. SHAW, H. N. *Surg., Gynec. & Obst.*, 1922, 34, 394.
6. WARD, GEORGE G. *Kelly's Gynecology*. Ch. xix. New York: D. Appleton and Co., 1928.
7. WATKINS, T. J. *J. Gynec. & Obst.*, 1899, 15, 520.
8. WATSON, B. P. Discussion. *Am. J. Obst. & Gynec.*, 1932, 24, 945.

# EDITORIALS

## SURGERY GYNECOLOGY AND OBSTETRICS

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### DIVERSION OF URINE ABOVE LEVEL OF BLADDER

IN the not too distant past a very considerable number of patients with bladders wrecked beyond repair have either lived in grave discomfort or even torture or gone to their deaths from renal insufficiency and infection. During the past 15 years much attention has been paid to various methods of diverting the urine all of them presenting some difficulty and therefore requiring a considerable period of study in order to assess their value. Although there are many patients for whom such procedures are desirable, the number coming under the observation of any one surgeon is rarely large enough to warrant conclusions except after the lapse of considerable time. Furthermore we are concerned here not with immediate results, not with mortality but with morbidity and late and permanent results. The lapse of time and the accumulated experience seems to me now to warrant some statement in regard to the place of these various procedures.

Granting at the outset that the bladder is either worthless, as in the cases of the extreme congenital deformities of exstrophy and com-

plete epispadias, or damaged beyond repair by inflammatory processes, such as chronic interstitial cystitis and tuberculous, or threatening death from a lesion of its own, as in the case of cancer some diversion of the urine with or without cystectomy—indicated rarely except for exstrophy and cancer—is clearly indicated.

We have at our disposal three methods: nephrostomy, uretero-enterostomy and cutaneous ureterostomy.

Nephrostomy may be used as an intermediate step in the re-arrangement of damaged ureters in which temporary diversion is indicated. It is, I believe, rarely the best method for permanent diversion since it is not notably more certain to preserve the integrity of the kidney and is more inconvenient than cutaneous ureterostomy.

There remain therefore the two other methods, implantation into the bowel or implantation into the skin. It is interesting to note that the mortality and immediate results of uretero-enterostomy have apparently been importantly better in the United States than in Europe where the operation has been considerably abandoned by many eminent experts on the ground of its high mortality which has often been in the neighborhood of 50 per cent. As compared with this there are considerable series of cases in this country showing a mortality below 5 per cent. This difference has arisen I think from the different selection of patients. Space does not here permit a discussion of the principles of selection, but it seems to me quite clear that the cases suitable for uretero-enterostomy will be almost invariably those in which the ureters are substan-

tially normal, and that the attempt to transplant grossly abnormal ureters is likely to be followed by a much higher mortality and less satisfactory results

For patients with normal ureters, where the operation can be done by moving one ureter at a time, the mortality and immediate results are satisfactory. The morbidity and end-results, although still in doubt, show, I believe, that the kidneys continue to function reasonably satisfactorily over periods in excess of ten years. On the other hand, there is no convincing array of cases showing that the kidneys remain strictly within normal limits after transplantation of the ureters by any method. We ought not to assume on the basis of the present evidence that uretero-enterostomy enables the patient to continue indefinitely with an entirely normal upper urinary tract. Some degree of dilatation almost universally associated with some degree of infection is the rule.

For the patients with grossly abnormal ureters, cutaneous ureterostomy has, I think, been shown to have a lower mortality and a relatively satisfactory result. Many of these patients already have infected kidneys. All of them—by definition—will have some dilatation of pelvis and calyces. If the operation is technically well carried out, and particularly if a fair sized catheter is kept permanently in the ureter up to the level of the renal pelvis, these patients are dry, comfortable, and can live effective lives.

Briefly summarized, nephrostomy is at its best in draining the kidney while some rearrangement of the ureter can be planned. Uretero-enterostomy is at its best where the ureters are normal, and will be most useful in congenital anomalies, in certain injuries of the bladder, and in a few cases of chronic interstitial cystitis. It may be used as a preliminary to total cystectomy for cancer, but will

here carry a higher mortality, since both ureters must be moved at the same time, and it is desirable to do the cystectomy either at the same sitting or after a brief interval. This is a grave surgical undertaking. Cutaneous ureterostomy is at its best in cases in which the bladder has ceased to be useful as a result of intolerable tuberculous cystitis, in other types of inflammation with dilatation of the ureter, in some cases of neuromuscular dysfunction, and in those cases of cancer of the bladder in which, although the ureters are obstructed and dilated, relief is still worth trying for or total cystectomy is still regarded as possibly curative.

HUGH CABOT

## A NEW BLOOD SUPPLY TO THE HEART BY OPERATION

THE human heart entered the domain of surgery in 1895 when Cappelen sutured a stab wound, the first operation of its kind on a human being to be recorded. At that time the attitude of the profession toward this operation was not uniformly favorable. Stephen Paget felt that surgery of the heart offered no prospect for development. This attitude can be understood when one contemplates the opportunities for the development of operative surgery offered by other organs during that early part of the aseptic period. Why should one be interested in the heart as a surgical organ when there were so many fruitful fields of endeavor? And so the decades have gone by. What has been accomplished in cardiac surgery has to a large extent been the result of sporadic interest. A few important contributions have been made, but in general it can be stated that the heart has not received very much sustained study by surgeons. The reason for this dearth of surgical endeavor is obvious. What could one hope to accomplish in this field?



My associates and I have worked with the problems of cardiopericardial surgery for a dozen years. For a long time it seemed as though we were working in a blind alley and all that we could accomplish in the first few years was to make observations and from this study to formulate a point of view concerning surgical problems. One of these observations was to note the presence of blood vessels in tissues that were adherent to the heart, an observation of no special significance at the time it was first made. After the lapse of several years a band of scar extending from the left ventricle was transected in a human patient. *Brisk bleeding occurred from each cut surface.* Here was evidence, the first of its kind to be recorded, that adherent tissues could and actually did transport blood to the human pulsating heart. A new significance was attached to this observation because in the intervening years we were attempting to give the myocardium a new source of blood supply.

According to our point of view the correctness of which seems quite obvious, the heart is anchored in the body. It is anchored by the walls of the great vessels by a little fat, a few nerves and a few lymphatics, and these structures are relatively avascular tissues. Because of this anatomical arrangement the heart has been deprived to a great extent of an important compensatory property namely the ability to develop a collateral circulation to meet an emergency to preserve life during the first few moments, hours, days, and weeks after a serious coronary accident. The appalling incidence of sudden death in our adult population attests to the destructive nature of coronary closure.

The experiments on this subject, done in collaboration with Dr V L Tichy and Dr Alan R

Moritz, consisted of the destruction of the mesothelial envelope around the heart and the construction of a vascular bed from which the heart could obtain a new source of blood supply. In these experiments the epicardium and mesothelial lining of parietal pericardium were removed. Tissues were then brought into contact with the myocardium. These tissues consisted of fat, fibrous pericardium, pedicle grafts of skeletal muscle and omentum. A physiological need for blood in the myocardium was produced by occluding the coronary arteries by silver bands which were placed around the arteries close to their aortic ostia. These bands were compressed in successive stages until the arteries were completely occluded. Complete occlusion of both coronary arteries was achieved experimentally with recovery and when the extracardiac vascular bed was injected with dye the myocardium became diffusely and intensely stained. It was concluded from these experiments that the heart was given a new source of blood supply.

Supplementary facts bearing upon the subject were established by experiments conducted in collaboration with Dr Ernest Bright and Miss Alice B Maltby. It was shown by these experiments that the presence of a collateral vascular bed adherent to the myocardium protected the heart against sudden occlusion of the right coronary artery. The degree of protection was not always sufficient to withstand complete occlusion of this artery in one stage, but the collateral bed had some prophylactic effect. When the ramus descendens of the left coronary artery was occluded in one stage, the prophylactic effect of the vascular bed was less marked. It was concluded from these experiments that the larger the coronary artery occluded the less the prophylactic effect.

It was also found that the right coronary artery the descending ramus of the left or the

It may be of interest to note that over 100 operations on the heart have been carried out in the Surgical Laboratory of the Harvard Medical University School of Medicine.

circumflex ramus of the left coronary artery could be ligated with almost uniform success if the occlusion were carried out in two stages. It was also learned by experiment that localized ischemia of the myocardium was highly fatal. Ligation of four or five peripheral branches of the coronary arteries over the apex of the left ventricle was uniformly fatal. The reduction in coronary blood flow brought about by this type of peripheral ligations was not great when compared to the total amount of blood passing through both major coronary arteries. A much greater reduction in the total coronary blood flow could be tolerated by the heart provided the constriction of the arteries was central rather than peripheral. This observation introduced the subject of distribution of blood flow in the heart—a subject of vital importance. The following demonstration was carried out. A collateral bed was applied to the myocardium and the right coronary artery was occluded completely. Several months later the left coronary artery was injected with dye. In this experiment the dye spread diffusely throughout both ventricles, while in a normal heart the dye did not penetrate the wall of the right ventricle. Not only was the right ventricular wall injected with dye but the dye flowed freely from the cut surfaces of the collateral bed. From this type of experiment it can be stated that the collateral vascular bed not only can bring blood into the myocardium from extracardiac sources but also it can transport blood from the bed of a coronary artery where the circulation is good to the bed of an artery where the circulation is deficient. In this respect the collateral bed can function as an anastomotic bridge which can bring about an equal distribution of blood to various parts of the myocardium.

During the last two years a series of experiments has been carried out in collaboration with

Dr. Robert Hosler and Dr. John Williams concerning the effect of adhesions upon the heart. While this work is still in progress, nevertheless, it can be stated that intrapericardial adhesions are silent, i. e., they produce no clinical manifestations of circulatory embarrassment. It can also be said that extrapericardial adhesions are silent, and that while both of these lesions combined can increase the work load of the heart, still these combined lesions usually, but not always, are silent. A second way in which extrapericardial and intrapericardial adhesions combined can affect the circulation is by angulating the heart from its normal axis. A third possibility is by the development of cardiac compression, but in this condition the compressing scar is the detrimental factor while adhesions, when present, are entirely silent and incidental. In general it can be stated that the importance of cardiac adhesions has been greatly overemphasized in the past. In most cases they produce no circulatory embarrassment whatsoever.

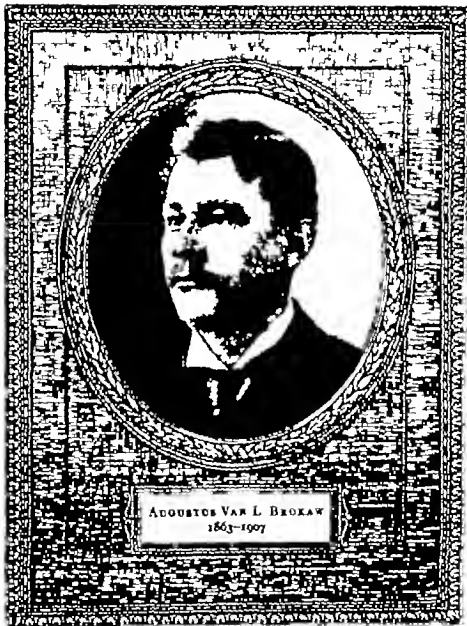
With these experimental data as a background, it was decided to try to apply them to human patients. The operation, the first of its kind, was done February 13, 1935. The insertion of the left pectoral muscle was incised to mobilize the muscle. The muscle was also cut to the left of the sternum. The epicardium was removed as was also the lining of the parietal pericardium. The pectoral muscle and the left internal mammary artery were brought onto the surface of the heart. Over five months have elapsed since this operation was carried out, and the patient claims that he is better. His feeling of substernal oppression has disappeared. He states that the sharp pain down the left arm has disappeared, that his feeling of impending death has gone. [He is now employed as a gardener. I have carried out] the operation in three additional patients. These patients tolerated the

operation, although one developed a thrombosis on a calcified plaque at the bifurcation of the aorta a week after the operation. The other two are living and apparently improved. Up to the present time we have had no deaths from the technical aspects of the operation.

In conclusion it should be said that while the myocardium has been given a new source of blood supply experimentally it cannot be said that the experimental data have been adequately applied to patients suffering from coronary sclerosis. The operation will have to be applied to a number of patients before

it will be known how beneficial it will be. Until this has been accomplished the operation should be looked upon as an experimental procedure. It is my belief however that this operation is going to open up a new field of surgery. It was my desire to withhold presenting this work until the results of the operation as applied to patients were definitely known. Unfortunately this was not possible. The operation is not without hazard, and it is my sincere hope that surgeons will not accept and apply this operation to human patients until the results are known. CLAUDE S. BUCK.





AUGUSTUS VAN L. BROKAW  
1863-1907



ington University he took the chair of clinical surgery and when Dr. Prewitt retired in 1902 Dr. Brokaw was chosen surgeon in chief to St. John's Hospital, which was also affiliated with Washington University.

Then in 1903 the St. Louis University established its School of Medicine by purchasing the Marion Sims-Beaumont Medical College, and immediately sought the assistance of several Roman Catholic hospitals in providing clinical instruction for its students. The control of the medical staff of St. John's Hospital was promptly and properly transferred to the administration of the newly acquired Jesuit school, and Dr. Brokaw accepted the chair of clinical and operative surgery in the St. Louis University Medical School and thereby remained at the hospital as its surgical chief. He retained these connections until he died suddenly 4 years thereafter of a gastric hemorrhage, on January 25, 1907.

When the street railways of St. Louis were fused into one huge organization Dr. Brokaw had already functioned as surgeon for several independent street car lines and although still "in the thirties," he was appointed chief surgeon to the citywide transit system. A half dozen or more of his full time assistants were housed in the spacious office building attached to his residence, first at Compton Avenue and Washington Boulevard and later in more commodious quarters on Taylor Avenue. By day and night some of these were always ready to answer emergency calls. Then, too, there were scores of privately practicing physicians distributed throughout the area of St. Louis who had been appointed for part time duty. On the whole, this corps was quite efficient.

Brokaw installed an X-ray apparatus almost immediately after he saw Professor Charles O. Curtman first demonstrate the new discovery of Professor Roentgen in Professor Nipher's Laboratory at Washington University in 1896. He foresaw its great value to medicine and especially to industrial and traumatic surgery. On account of the frequent changes and improvements in the early models of coils and tubes he was kept busy discarding various pieces of apparatus and replacing them with others of greater efficiency. His name should be inscribed high up on the honor roll of pioneer roentgenologists.

A. V. L. Brokaw was a stickler for asepsis, by enforcing thorough heat sterilization of surgical instruments, linens, etc. to obtain an aseptic operative field at a time when most surgeons were still indifferent or careless in such matters. These precautions, coupled with the confidence in his own dexterity with a scalpel and his extensive knowledge in anatomy are responsible for many recoveries which might have terminated otherwise. He had many admirers among the younger physicians, and was a popular consultant and operator with them.

Sometimes brusque and apparently blunt in demeanor, our subject was decidedly cordial and communicative to whomever he trusted and respected, even if that individual was his junior by many years. In his private work, as well as in his corporate practice, the question of remuneration was always secondary.





# LANDMARKS IN SURGERY

## NICHOLAS SENN'S WORK IN EXPERIMENTAL SURGERY AND SURGICAL PATHOLOGY AND ITS INFLUENCE ON THE SURGERY OF HIS TIME

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THE work of Nicholas Senn is an important landmark in American surgery. It is my purpose to present a brief sketch of the late Nicholas Senn and his work in experimental surgery and surgical pathology and its influence on the surgery of his time. I am delighted to do this as I knew Senn very well and followed with great interest his surgical work, both his research work and his teaching. In the period that I was an associate of his in the Rush Medical faculty from 1884 to the time of his death in 1906 Senn had a striking personality. He was a fine looking man of medium height, large head and large torso, and gave one the impression of great physical and mental power.

Garrison who has written such an admirable history of medicine gives the following brief account of Nicholas Senn:

Nicholas Senn (1841-1906), of Berlin, Switzerland, emigrated to the United States in 1857, graduated from the Chicago Medical College (1864) and became professor of surgery at the Rush Medical College of that city. Senn was highly trained, scientific surgeon. He made valuable experimental contributions to the study of aneurysms (1873), the surgery of the pancreas (1886), gunshot wounds, and intestinal anastomosis, in which he introduced the use of decalcified bone plates. He was, in fact, great master of intestinal surgery, especially in the surgical development of the treatment of appendicitis. His devotional method of deflecting intestinal perforation by means of incision from the incision with hydrogen gas (1891), and was the first to use the foreign body in the treatment of aneurysms (1891). Senn played an important part in the Spanish American War, founded the Association of Military Surgeons of the United States (1891) and, at his death, left a fine collection of medical books to the University Library and other handsome bequests to the city of his adoption.

In 1857 following the death of Moses Gunn, the professor of surgery at Rush Medical College, Nicholas Senn and Charles T. Parley were elected to succeed him. Senn's career had been an interesting one. After he graduated from medical school and after serving his internship at the Cook County Hospital he had gone to small towns in Wisconsin where he began the practice of medicine. From there he moved to Milwaukee where he built up a very large general practice and at the same time established a reputation as an excellent surgeon. In

1877 he went to Munich where he received training in surgical pathology and clinical surgery. After his return to Milwaukee he came to Chicago to see each week to give a clinic on the principles of surgery at

the University of Illinois Medical School. At the same time he began his experimental work in connection with gunshot wounds of the abdomen, intestinal repair and surgery of the pancreas. Together with Parley he did a great deal to solve the problem of the proper handling of gunshot wounds of the abdomen. The report of his large series of experiments upon the repair of abdominal wounds was published in the *Annals of Surgery*. In addition Senn developed various plans of diagnosis in intestinal lesions, a very ingenious one being to inflate the bowel from below with hydrogen gas and then locating the intestinal tear by lighting the escaping gas. At the same time he was engaged in experimental work which led to the development of his celebrated bone plates.

In 1887, Senn spent a month visiting the important English, Scotch, and European clinics and wrote letters presenting quite fully his experience in these various clinics to his great friend, Christian Fenger. Christian Fenger had these letters printed in the *Journal of the American Medical Association*. After his return the American Medical Association published a little volume of these letters, entitled "Four Months Among the Surgeons of Europe."

In order to form a good conception of Senn's work and Senn's career I think it is necessary to visualize the stage of the development which surgery had reached in Senn's time. Senn graduated from the Chicago Medical College in 1866, one year after Lister had published his first paper on antiseptic surgery that was in 1867. Before that time surgery and medicine were in a fog, in a mist, one could not say that medicine was yet a science, but with Lister's work we had at least scientific foundation upon which to build surgery. It should be remembered that when Lister presented his conception of antiseptic surgery it was but theory based on Pasteur's demonstration that fermentation was result of minute organisms. Influenced by this demonstration of Pasteur, Lister came to the conclusion that suppuration was due to the introduction of minute organisms into an open wound. He knew from experience that in a closed fracture suppuration did not occur, that in a compound fracture suppuration was the rule. He believed that in the open fracture minute organisms floated from the air into the

wound or were introduced into the wound by contact with the fingers or dressings or instruments that come in contact with it. Younger men can hardly realize the opposition, even the ridicule, that met Lister's suggestions.

Although Lister's paper on the antiseptic treatment in surgery was published in 1867, his suggestions were only very slowly accepted. Lucas-Championnière in France and Thiersch and Volkmann in Germany adopted Listerism in the early seventies. Lister's work was based at first upon the theory that germs produced suppuration and he sought to exclude them from the wound. These pus germs were not demonstrated until Ogston, in 1881, Rosenbach, somewhat later, and Koch, finally, with solid media were able to grow pure cultures of staphylococci and streptococci and

prove conclusively the fact that these pus organisms were the cause of suppuration. In this uncertain period of about 15 years, the majority of the surgeons of the world refused to accept Lister's theory.

In looking over the literature of the period when Senn began his surgical work, in order to visualize the surgery of this time, I find nothing that compares with a publication of Billroth's in which he reports the work which he did in his surgical clinic at Zurich and his surgical clinic in Vienna from 1860 to 1876 (*Chirurgische Klinik*, Dr Th. Billroth, Berlin, 1879). During the sixteen-year period covered in Billroth's report he handled 9,508 cases and had 785 cases of erysipelas and pyemia and a few cases of tetanus, making about 8 per cent of accidental wound infections. Of 1,076 patients who died, 477 died of wound infection. He operated on 77 patients with breast carcinoma and removed the mammary glands with the axillary glands, of these 77 patients, 24 died, 3 from secondary hemorrhage, 1 from pneumothorax on the evening of the operation, and 10 each from erysipelas and pyemia. In his report on his amputations, resections, and osteotomies of the extremities, he operated on a total of 214 cases, of these 150 recovered and 64 died, 9 from collapse, 3 from erysipelas, 2 from delirium tremens, and 50 from septicopyemia—a mortality of 29.9 per cent. Billroth reports that up to February, 1879, he had done 140 ovariectomies, of these 83 patients recovered and 57 died—a mortality of 30.71 per cent. With this terrible mortality we wonder how



Nicholas Senn, 1844-1908

the surgeons of 1880 had the courage to continue to operate. What a marvelous revolution was brought about by Lister! What a change came with the general introduction of sound antiseptic surgery!

In 1889, on his return from abroad where he had had the opportunity of studying bacteriology, Nicholas Senn published an admirable book on surgical bacteriology which ran through several editions and a year later published his textbook on *Principles of Surgery*. I am quite sure that this book had a very important bearing on the development of American surgery. It was the first book of its kind published in English. In Germany admirable books on the "Principles of Surgery" had been published by Koenig and Billroth. Many of our American and English surgeons devoted their time almost entirely

to the practical side of surgery and had neglected the underlying principles. I remember John Chiene (professor of surgery at Edinburgh), whom I met shortly after this volume was published, told me that Senn's book on *Principles of Surgery* had led him to change completely his course of surgical instruction at Edinburgh and he adopted the book as the textbook for his classes. Senn later published a book on *Tumors, Their Surgical Aspects*.

The years from 1880 to 1900, which cover the most important period of Senn's career, were the two decades which witnessed the great development from the old surgery into modern scientific surgery, and Senn took a more important part in this development during these 20 years than any other American surgeon. Senn was considered for the position of professor of surgery at a number of institutions, among others, for the chair of surgery at Johns Hopkins when they were first organizing their faculty and before Halstead received the appointment, and later for the professorship at the University of Pennsylvania.

After he was made the head of the surgical department at Rush Medical College, Senn gave one of the most instructive clinics I have ever listened to. He was perfectly familiar with many of the best surgical clinics in Europe and in Great Britain, and he modeled his own clinic after the surgical clinics of the German universities. He gave two clinics a week. They began promptly at two o'clock in the afternoon. The large upper amph-

theater at Rush College which had a seating capacity of about four hundred was as a rule crowded with students and visitors. Senn would first show gross and microscopic specimens from cases in which operation had been done usually at the preceding clinic. He laid great stress on a thorough knowledge of surgical pathology and bacteriology then he would present patients from the hospital and the dispensary make careful examinations and diagnoses, and would discuss the treatment which he thought was indicated in each case. This work would fill the time from about two to four o'clock. Then he would begin operating and, as a rule, had a long list of cases, three, five or seven, and he would continue operating until six o'clock, sometimes even until seven o'clock, and the majority of the students and visitors would remain throughout this long clinic. These clinics were always found to be most instructive and profitable.

Senn was very familiar with medical history. He had traveled so extensively through European countries that he had met personally many of the prominent surgeons so that he could give a very good presentation of the history of an operation, the man who had introduced it and the results which he had obtained, so that one could visualize from his clear cut discussion very clearly the evolution of modern surgery. Senn also introduced into the clinic the plan which is customary in the German clinics of calling down student consultants, having them examine personally the cases, stating what they had found, their diagnoses, and their suggestions as to

treatment. Senn constantly emphasized the importance of surgical research and experimental surgery in the development of clinical surgery.

Senn was very positive in his statements and gave very definite directions in regard to diagnosis and therapy. Some men considered this a fault as a matter of fact it was an evidence of strength because a great surgical teacher must be definite, clear and emphatic, if he is to be of the greatest service to his students. Lord Mayo, who is probably more familiar than any other British surgeon with American surgery, stated recently in discussing American surgery that the two greatest teachers of surgery in America he had met were Nicholas Senn and John B. Murphy.

A prolific writer with a list of 36 books and articles to his credit, Senn presented the greater part of his work before meetings of the various medical and surgical associations in this country and abroad. Taking part in a symposium upon peritonitis, Senn stressed to his colleagues the importance of early operation, the removal of the source of the peritonitis, the advantages of rapid operation, and the startling improvements to be obtained from the use of large amounts of fluids administered subcutaneously. It is interesting that when at this day one reads his works, a picture of modern scientific surgery is presented far beyond the boundaries of the common surgical practice of his time. The surgical profession in this country should be proud of Nicholas Senn and of the great service which he rendered to medicine and surgery.

# CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

ROBERT B GREENOUGH, Boston, *President*

DONALD C BALFOUR, Rochester, *President-Elect*

HOWARD C NAFFZIGER, *Chairman*, THOMAS F MULLEN, *Secretary, Committee on Arrangements*

## PRELIMINARY PROGRAM FOR THE 1935 CLINICAL CONGRESS

FOR the twenty-fifth annual Clinical Congress of the American College of Surgeons, to be held in San Francisco and Oakland, October 28-November 1, the surgeons of that great medical center on the Pacific coast have organized under the leadership of a strong and representative committee and have prepared a program of clinics and demonstrations that will provide a complete showing of their clinical activities in all departments of surgery. The Committee on Arrangements has been assured of the hearty co-operation of the clinicians at the medical schools and twenty-seven hospitals that will participate in the program.

The clinical program, published in tentative form in the following pages, is to be further revised and amplified during the coming weeks as the work of the program committee progresses. Operative clinics and demonstrations in the hospitals are scheduled for the afternoon of Monday, October 28, beginning at 2 o'clock, and for the mornings and afternoons of each of the four following days. The real program will be published daily during the Congress—a complete and accurately detailed program which will be posted in the form of bulletins at headquarters each afternoon for the succeeding day. The same material will be issued in printed form the following morning.

Special features of the clinical program include (1) Cancer clinics demonstrating the treatment of cancer by surgery, radium and X-ray, (2) fracture clinics demonstrating modern methods of treatment, (3) clinics in traumatic surgery demonstrating the newer methods of rehabilitation of injured patients by surgery and physiotherapy.

Surgical motion picture films, both sound and silent, will be exhibited daily at headquarters at the Fairmont Hotel. Such surgical film exhibitions have met with popular acceptance in recent years,

and an extensive exhibit, including many new films, is planned for this year's Congress.

### EVENING MEETINGS

A tentative outline of the programs for five evening sessions, as prepared by the Central Executive Committee, is presented in the following pages. At the presidential meeting on Monday evening in the War Memorial Opera House the retiring president, Dr Robert B Greenough, of Boston, will deliver the annual address followed by the inauguration of the new officers—Dr Donald C Balfour, Rochester, Minn., president, Dr Arthur W Allen, Boston, and Dr John A Gunn, Winnipeg, vice-presidents. The annual oration on surgery will be delivered by Dr George Crile, of Cleveland, Chairman of the Board of Regents. His subject will be "The American College of Surgeons—Past, Present and Future."

On Tuesday, Wednesday and Thursday evenings scientific sessions will be held in the Auditorium of the Veterans' Building at which eminent surgeons of the United States and Canada, together with visiting surgeons from foreign countries, will present and discuss papers on surgical subjects of timely importance.

At the annual convocation, to be held in the War Memorial Opera House on Friday evening, the 1935 class of candidates will be received into Fellowship. The president, Dr Donald C Balfour, will deliver his inaugural address on this occasion, and the Fellowship address will be delivered by Robert Gordon Sproul, B S, LL D, president of the University of California.

### HOSPITAL CONFERENCE

The eighteenth annual hospital standardization conference will open with a session in the Gold Ballroom of the Fairmont Hotel at 9.30 on Monday morning at which addresses will be delivered

by distinguished representatives of several organizations. At this session the annual report of the hospital standardization activities of the College for 1935 including the list of approved hospitals, will be presented.

Monday afternoon will be given over to a discussion of hospital problems from various aspects in which administrators, surgeons and others will participate.

Tuesday morning will be devoted to a panel discussion of the hospital's obligation to its community and its part in the community life professionally and economically.

A joint session with the Association of Record Librarians will be held on Wednesday morning at which problems concerning hospital records are to be discussed.

Tuesday and Wednesday afternoons will be devoted to definitely planned departmental demonstrations in hospital administration in certain of the San Francisco hospitals. These demonstrations will show how various departments function, affording those present an excellent opportunity to see how other institutions carry on their activities.

Thursday will be Oakland Hospital Day and a program of demonstrations of special interest will be carried on in four of the major hospitals in Alameda County with the co-operation of the Oakland Hospital Council. Many new features and procedures in hospital management will be demonstrated.

Through the courtesy of Dr. D. W. Black, medical director of the Highland Hospital and director of Alameda County health activities, those who are interested in the Alameda plan for medical and hospital care will be given an opportunity to make an excursion through the county on Friday.

#### FRacture CONFERENCE

A conference on fractures will be held under the auspices of the College Committee on the Treatment of Fractures on Tuesday afternoon at 3 o'clock in the Gold Ballroom of the Fairmont Hotel. The chairman's report will include a summary of the activities of the Committee and the accomplishments of its regional committees throughout the United States and Canada. Papers are to be presented as follows:

FREDERIC W. BARNHART, M.D. New York, Chairman of Committee on Treatment of Fractures, presiding  
Highway First Aid Stations. E. P. YALE PALMER, M.D. Phoenix, Arizona  
Fracture Fixtures into the Knee Joint. FREDERIC J. COY, M.D. Boston  
Status of Fractures in the Field of Surgery. CLAY RAY MERRA, M.D. New York.

Local Anesthesia in Fractures. E. DUFFELL MERRILL, M.D. Chastanoot, Tenn.  
The Causes of Non-Union; Bone Growth and Regeneration. WILLIAM R. OSBORN, M.D. Chicago.

#### CANCER SYMPOSIUM

The symposium on cancer under the auspices of the College Committee on the Treatment of Malignant Diseases, will be held on Thursday afternoon in the Gold Ballroom of the Fairmont Hotel following the annual meeting of the Fellows. The symposium will concentrate on the standard accepted methods for the treatment of cancer.

A report on five-year results of therapy compiled by the Department of Clinical Research continuing the gathering of statistics on this subject from clinicians in various parts of the United States and Canada during the past several years, will be included.

CHARLES A. DUTCH, M.D. Oakland, Calif. Chairman of Committee on the Treatment of Malignant Diseases, presiding.

PROSTATE. BENJAMIN S. BARKINGER, M.D. New York.  
FRENCH DUTCH. ALBERT R. KILGORE, M.D. San Francisco.  
COLON. THOMAS E. JONES, M.D. Cleveland.  
LARYNX. GORDON B. NEW, M.D. and F. A. FLETCHER, M.D. Rochester, Mass.  
MELANOMA. FRANK E. ADAMS, M.D. New York.  
A Diagnostic Cancer Clinic in Private Hospital. C. HIRSH WEAVER, M.D. Los Angeles.  
Five-Year Results of Treatment. BOWMAN C. CROWELL, M.D. Chicago.

#### CONFERENCE ON INDUSTRIAL MEDICINE AND TRAUMATIC SURGERY

The Board on Industrial Medicine and Traumatic Surgery will hold its annual conference on Friday afternoon at 3 o'clock in the Gold Ballroom of the Fairmont Hotel. The program includes a report on the activities of the College in conducting investigations and surveys among industrial establishments during the past year in continuation of the work done along these lines during the past five years.

FREDERIC A. BOWLEY, M.D. Washington, D.C. Chairman of Board on Industrial Medicine and Traumatic Surgery, presiding.

Edison and Its Control. R. R. BAYNES, M.D. and R. R. JONES, M.D. Washington.  
Analysis of Fore Handled Injuries under Steel Operations. SURVEY WALKER, J. M.D. Chicago.  
Tissue Acid and Silver Nitrate in Burns. ADALBERT BREITMAN, M.D. Chicago.  
Heat Exhaustion and Its Prevention. LOYAL A. SMITH, M.D. Bethlehem, Pa.  
Immediate and Delayed Repair of Trauma Injuries. MICHAEL L. MARON, M.D. Chicago.  
Report of the 1935 Survey of Medical Services in Industry by the American College of Surgeons. M. N. NEWCOMB, M.D. Chicago.

## OPHTHALMOLOGY AND OTOLARYNGOLOGY

The committee in charge of the section on surgery of the eye, ear, nose and throat has arranged a program of ophthalmological and otolaryngological clinics and demonstrations at the hospitals and medical schools, as published in tentative form in the following pages. Scientific sessions will be held at the Fairmont Hotel on Tuesday, Wednesday, Thursday and Friday mornings, at which papers are to be presented as follows:

- Relation of Orthoptics to the Surgical Treatment of Concomitant Strabismus. A. D. PRANGER, M.D., Rochester, Minn.  
 Title to be announced. CLIFFORD B. WALKER, M.D., Los Angeles.  
 Surgical Correction of Defects Due to Paralysis of the Muscles of the Eyes or of the Eyelids. MEYER WIENER, M.D., St. Louis.  
 What the General Public Should Know About the Eye. J. O. McREYNOLDS, M.D., Dallas, Texas.  
 A New Indosclerectomy Operation for Glaucoma. CONRAD BERENS, M.D., New York.  
 Analysis of Five Hundred Intra Ocular Steel Operations. SYDNEY WALKER, JR., M.D., Chicago.  
 Brief Consideration of the History of the Development of Mastoidectomy. ROBERT SONNENSCHNEIN, M.D., Chicago.  
 Title to be announced. F. E. LEJEUNE, M.D., New Orleans.  
 Cancer of the Larynx. W. E. SAUER, M.D., St. Louis.  
 Surgical Approach to the Nasal Accessory Sinuses. WILLIAM MITHOEFER, M.D., Cincinnati.  
 Selection of Treatment for Malignancy of the Upper Respiratory Tract. FREDERICK A. FIGI, M.D., Rochester, Minn.  
 Unique Symptoms and Effects of Sphenoidal Empyema. CHESTER H. BOWERS, M.D., Los Angeles.

## COMMUNITY HEALTH MEETING

Following its established custom and in recognition of its obligation to the public to provide authoritative information on modern surgery, better hospitals, and the prevention of disease, a community health meeting will be held on Wednesday evening at 8 o'clock, under the auspices of the American College of Surgeons, in the Exposition Auditorium, presenting a program appropriate for the occasion and consisting of brief interesting talks on scientific medicine, health, and hospitals, also a motion picture film on a medical subject of interest to the laity.

## ANNUAL MEETING

The annual meeting of the Fellows of the College will convene in the Gold Ballroom of the Fairmont Hotel at 2 o'clock Thursday afternoon. Reports by the officers and chairmen of the standing committees on the various activities of the College will be presented, followed by the election of officers.

## MEETING OF NEW FELLOWS

Candidates for fellowship in the American College of Surgeons, class of 1935, will assemble in the Gold Ballroom of the Fairmont Hotel at 11 a.m. on Friday for the necessary instructions previous to receiving their fellowships and to sign the fellowship roll.

## A VACATION ON THE PACIFIC COAST AND THE CLINICAL CONGRESS

Many Fellows of the College and their guests, who will attend the Clinical Congress in San Francisco in October, are planning to take advantage of the opportunity which naturally suggests itself to include a vacation and sight-seeing trip on the Pacific coast. All the railways are offering very low round-trip rates with liberal stopover privileges from all parts of the United States and Canada, with the added privilege of traveling to the coast by one route and returning by another, thereby affording unusual opportunities for visiting many points of interest en route.

When nature fashioned the Pacific coast she was in a spendthrift mood. From the Canadian border to the Mexican line she scattered her beauties and wonders with a prodigal hand—mountains, rivers, waterfalls, oceans, beaches, forests, lakes, even a live volcano, the only one in the United States.

Few cities have so impressive a setting as San Francisco. The rugged hills upon which it is built, the Golden Gate, Mt. Tamalpais, the misty bay to the east, Oakland and Berkeley, and the hills beyond, all contribute to its grandeur. It is a pleasing picture and the citizens of San Francisco have not been unmindful of it. Their parks and residence districts have a dignity and beauty in keeping with the scene about them.

The glamour of the city is inescapable, but no amount of description can picture accurately this unique city. One must see for himself how the many charming aspects of San Francisco and its environs blend into one delightful and unforgettable picture.

Along the Pacific coast one will find much to claim his attention. First, there is the California-Pacific International Exposition at San Diego—a World's Fair of magnitude, with many important medical and other scientific exhibits—erected in Balboa Park, a tropical fairyland. The buildings, which are permanent structures, have their dignity and beauty enhanced by the gorgeous setting.

Los Angeles with its mountain background, its broad boulevards, its nearby beaches, its hospitality—and Hollywood—afford opportunities for

entertainment and recreation. A one-day trip to enchanting Catalina Island, with its balmy south sea island atmosphere would naturally suggest itself.

Traveling south but a short distance from San Francisco, one enters the San Joaquin valley at Merced—the gateway to Yosemite National Park, where one views one of the most famous spectacles of nature. The valley occupies but eight square miles, but in this limited space are gathered more natural wonders than can be found in any other similar area in the world. It contains eight waterfalls, the lowest twice the height of Niagara, and the highest the equal of ten Niagaras. There are meadows of deep grass and wild flowers, a rushing mountain river forests and towering cliffs. A short distance beyond is Sequoia National Park, containing thousands of giant Sequoia, the largest and oldest living things on the face of the globe.

Del Monte and Pebble Beach on the famous seventeen mile drive, are but a short distance from San Francisco. Other nearby points of interest are Paso Robles, with its almond groves, lovely Santa Barbara with its famous Old Mission, and a score of cities whose names are associated with the romantic Spanish period—a fairyland of natural and cultivated beauty.

To the north there are many cities to claim your attention. Vancouver in British Columbia, built up against mighty mountains with a primeval forest almost at its environs. Seattle, the great shipping center of the northwest, with Puget Sound to the west and beyond it the white-capped Olympics. In the distance the Cascade Mountains and looming to the southeast, Mt. Rainier held in special veneration by the Indians as the mountain that was God—no peak in the United States is so majestic. Portland, famous for its natural beauty—a literal bow of roses, the blue miracle of Crater Lake, Mt. Shasta and Lassen Peak, the only active volcano in the United States.

Traveling through the mountains one will enjoy the grandeur of the high Sierras, and a visit en route to the Mormon capital—Salt Lake City—will be a notable feature of the journey.

No matter what route one takes he will view a truly great and inspiring American scene—the thriving farm lands of the midwest, the noble stretches of prairie, the sublime mountain ranges of the Rockies, the grandeur of the desert, the towering forests of the far west, and then the blue Pacific.

This year one will travel in comfort and luxury undreamed of a short time ago. Whatever route one travels he will find his train air-conditioned.

This single factor adds so much to the comfort and pleasure of a trans-continental journey that it definitely and certainly marks the beginning of a new era in transportation history.

#### RAILWAY FARES FROM VARIOUS CITIES TO SAN FRANCISCO AND RETURN

Low round-trip fares will be in effect from all points in the United States and Canada. Consult your local ticket agent as to exact fare. Summer tourist tickets are good going via one route and returning via the same or any other authorized route with a final return limit of November 30.

	Round Trip Fare	Lower Rate One Way
Atlantic	\$ 00 75	\$ 5
Baltimore	30 75	24 00
Boston	25 80	5 85
Buffalo	109 55	5 25
Chicago	86 00	5 75
Cincinnati	97 00	9 50
Cleveland	94 35	9 50
Detroit	98 50	19 50
Denver	86 00	7 75
Kansas City	73 00	3 5
Memphis	85 5	4 50
Minneapolis	86 00	5 75
Montreal	35	24 75
New York	90 50	24 75
New Orleans	85 5	4 00
Omaha	7 00	13 75
Philadelphia	85	22 00
Pittsburgh	97	20 5
Portland, Ore.	30 70	5 50
St. Louis	8 50	5 00
St. Paul	86 00	7 75
Seattle	27 05	6 75
Toront	96 5	35
Vancouver B. C.	4 55	5 75
Washington	20 75	24 00
Winnipeg (via Portland)	50 00	5 75

#### ADMITTANCE REGISTRATION

The hospitals and medical schools of San Francisco and Oakland afford accommodations for a large number of visiting surgeons, but to insure against overcrowding attendance at the Congress will be limited to a number that can be comfortably accommodated at the clinics—the limit of attendance being based upon the result of a survey of the amphitheaters, operating rooms, and laboratories of the hospitals and medical schools to determine their capacity for visitors. It is expected therefore that those surgeons who wish to attend the Congress will register in advance.

Admittance to all clinics and demonstrations will be controlled by means of special clinic tickets, which plan provides an efficient means for the distribution of the visiting surgeons among the several clinics and insures against overcrowding, as the number of tickets issued for any clinic will

be limited to the capacity of the room in which that clinic will be given

A registration fee of \$5.00 is required of each surgeon attending the annual Clinical Congress, such fees providing the funds with which to meet the expenses of the meeting. To each surgeon registering in advance a formal receipt for the registration fee is issued, which receipt is to be exchanged for a general admission card upon his registration at headquarters. This card, which is non-transferable, must be presented in order to secure clinic tickets and admission to the evening meetings.

#### HEADQUARTERS—TECHNICAL EXHIBITION

Headquarters for the Congress will be established at the Fairmont and Mark Hopkins hotels. At the former the Terrace Ballroom and Foyer, the Gold Ballroom and other large rooms on the main floor and on the terrace have been reserved for scientific sessions and conferences, registration and clinic ticket bureaus, bulletin boards, exhibits, executive offices, etc. The Peacock Court and Room of the Dons at the Mark Hopkins will be utilized for various scientific sessions.

The Technical Exhibition, including the registration and clinic ticket bureaus, will be located in the ballroom and foyer on the terrace floor of

the Fairmont Hotel. In these rooms will also be found the bulletin boards on which the daily clinical program will be posted each afternoon. The leading manufacturers of surgical instruments, X-ray apparatus, operating room lights, hospital apparatus and supplies, ligatures, dressings, pharmaceuticals and publishers of medical books will be represented in this exhibition.

#### SAN FRANCISCO HOTELS AND THEIR RATES

In addition to the two headquarters hotels—the Fairmont and Mark Hopkins—there are a number of first-class hotels within short walking distance of headquarters providing ample hotel facilities at reasonable rates. The following hotels are recommended by the Committee:

	Minimum Rate with Bath	
	Single	Double
Bellevue, Geary and Taylor	\$3.00	\$4.00
Californian, Taylor and O'Farrell	3.00	4.50
Clift, Geary and Taylor	3.50	5.00
El Cortez, Geary near Taylor	3.00	4.50
Fairmont, Mason and California	3.50	5.00
Gaylord, Jones near Geary	3.00	4.00
Mark Hopkins, Mason and California	3.50	5.00
Palace, Market and New Montgomery	3.50	5.00
Plaza, Post and Stockton	3.00	4.00
Sir Francis Drake, Powell and Sutter	3.50	5.00
Stewart, 353 Geary	2.50	4.00
St. Francis, Union Square	3.50	5.00

## ANNUAL HOSPITAL STANDARDIZATION CONFERENCE

*Monday, 9 30-12 30—Gold Ballroom, Fairmont Hotel*

ROBERT B. GREENOUGH, M.D., Boston, presiding.  
Greetings: JACOB C. GEIGER, M.D., and LEON M. WILBOR, M.D., San Francisco

Introduction of distinguished guests

The Hospital Standardization Movement of the American College of Surgeons and Announcement of Approved List of Hospitals for 1935. GEORGE CRILE, M.D., Cleveland

The Hospital and the Changing Social Order. SISTER JOHN GABRIEL, R.N., Seattle, Wash.

Opportunities for the Training of Surgeons in the Approved Hospital. IRVIN ABEL, M.D., Louisville

Organization and Administration of an Oxygen Therapy Service in a General Hospital. R. C. BUERKI, M.D., Madison, Wis.

An Accredited Pathologist for Every Approved Hospital. PHILIP HILKOWITZ, M.D., Denver

The Future of the Voluntary Hospital. ROBERT JOLLY, Houston, Texas

Discussion. FREDERIC A. BESLEY, M.D., Waukegan, Ill.

*Monday, 2 00-5 00—Gold Ballroom Fairmont Hotel*

BENJAMIN W. BLACK, M.D., Oakland, presiding.  
Application of the Principles of Hospital Standardization from the Viewpoints of  
Hospital Trustee. W. C. CRANDALL, La Jolla, Calif.  
Hospital Administrator. PAUL H. FESLER, Chicago  
Medical Staff Member. JACOB F. HIGHSMITH, M.D., Fayetteville, N.C.

Clinical Pathologist. ALVIN G. FORD, M.D., Pasadena, Calif.

Radiologist. EDWARD S. BLAINE, M.D., Los Angeles  
Nurse. SISTER MARY STEPHANIE, R.N., San Francisco

Dietitian. LUCILE WAITE, San Leandro, Calif.  
Medical Social Worker. MARGUERITE L. SPIERS, Oakland.

Medical Educator. ALEXANDER R. MUNROE, M.D., Edmonton, Alta.

Economist. DANIEL CROSBY, M.D., Oakland

*Tuesday, 9 30-12 30—Gold Ballroom, Fairmont Hotel*

ARTHUR M. CALVIN, St. Paul, presiding.  
Innovations in Hospital Equipment and Supplies from the Standpoint of Efficiency, Economy, and Service.  
G. W. OLSON, Los Angeles

The Institutional Care of Chronic and Convalescent Patients. A. C. JENSEN, San Leandro, Calif.

Panel Discussion Conducted by JOSEPH G. NORBY, Minneapolis

To Create Understanding—Public Relations. FRANK J. WALTER, Denver

To Provide Adequate Service. G. WAITE CURTIS, San Francisco

To Bring the Cost of Hospital Service Within Reach of the People Served. R. E. HEERMAN, Los Angeles

To Provide Adequate Service to the Indigent Patient. J. V. BUCK, Spokane, Wash.



**T Educate Nurses, Doctors, and Others Engaged in the Care of the Sick.** CAROLIN E. DAVIS, Portland, Ore.

**Tuesday 10-5 00—St. Mary's Hospital**

Demonstrations and round table discussions dealing with methods of standardization and administration. Conducted by STORMA MAIR THOMAS, Superintendent, and heads of departments.

Business administration—equipment, personnel, accounting, reports, hospital costs, methods for solving present economic conditions.

Organization and management of food service—control and responsibility personnel, types of service, special diets.

Pharmacy service—organization and management, physical requirements, personnel, accounting.

Adjunct departments—Organization and management of chemical laboratory, X-ray and physical therapy departments, technical service, routine examination, records and filing.

**Tuesday, 8 00—10 30—St. Mary's Hospital**

Round Table Conference—A discussion of every day hospital problems as applied to the professional and economic aspects of hospital administration. Conducted by ROBERT JOLLY, Houston, Texas.

**Wednesday, 8 30-12 30—Gold Ballroom, Fairmont Hotel.** Joint Session with Association of Record Librarians of North America. R. C. BOTTRELL, M.D., Madison, Wis. presiding.

Section, Supervising, and Using Medical Records. MARCOLIN T. MACBACHER, M.D., Chicago. Discussion from the viewpoint of Hospital Administrator. THOMAS E. SWARTZ, M.D., Oakland.

Physician. S. MARK WHITE, M.D., Minneapolis. Surgeon. ALTON OCHSNER, M.D., New Orleans. Obstetrician. D. G. TOLLESON, M.D., Los Angeles. Ophthalmologist and Otolaryngologist. WILLIAM W. FLEMMING, M.D., Des Moines, Iowa. Record Librarian. MINNIE G. HILL, Los Angeles. Group Studies. Hospital to Scientific Efficiency. SUSAN M. SERVATTA, R.N., Kansas City, Mo.

**Wednesday 10-5 00—University of California Hospital.** Demonstrations and round table conferences on the organization and management of the medical records department. Conducted by F. S. DUNN, Superintendent, and heads of departments.

Physical requirements, personnel, supervision, filing and cross-indexing records, uses of records, special problems, standard nomenclature.

**Wednesday 10-5 00—San Francisco Hospital**

Demonstrations and round table conference on care of the obstetrical patient in the general hospital. Conducted by LAURENCE WILSON, M.D., Superintendent, and heads of departments.

Prenatal care, admission procedure, care of the patient in labor, delivery room technique, postpartum care, the isolated or septic patient, care of the newborn, follow-up and end results, review of morbidity and mortality, records. Motion picture. Around the Clock with You and Your Baby.

#### OAKLAND HOSPITAL DAY—THURSDAY

**10 00—10 30 p.m.—Providentia Hospital**

Demonstrations and round table conferences. Economics in hospital management. Staff of Providentia Hospital.

Organization and management of the housekeeping department. Staff of Fairmont Hospital.

Organization and functioning of the social service department. Staffs of Alameda County and Berkeley General Hospitals.

**10-5 00—Seward Merritt Hospital**

Demonstrations and round table conferences. Admission and discharge procedures. Staffs of the Seward Merritt and Peralta Hospitals.

Organization and management of central supply room. Staff of Seward Merritt Hospital. Hospital formulary. Staff of Peralta Hospital.

**Friday 10 00**

Inspection of the emergency system of the Alameda County Hospital and tour of county institutions for study of the Alameda plan.

## PRELIMINARY PROGRAM FOR EVENING MEETINGS

*Presidential Meeting—Monday, 8 15 p m—War Memorial Opera House*

Address of Welcome HOWARD C NAFFZIGER, M D , San Francisco, Chairman of Committee on Arrangements

Introduction of Foreign Guests

Address of the President The Conscience of the Surgeon ROBERT B GREENOUGH, M D , Boston

Inauguration of Officers President, DONALD C BALFOUR, M D , Rochester, Minn , First Vice-President, ARTHUR W ALLEN, M D , Boston, Second Vice-President, JOHN A GUNN, M D , Winnipeg

Annual Oration on Surgery The American College of Surgeons—Past, Present and Future GEORGE CRILE, M D , Cleveland

*Tuesday, 8 15 p m—Auditorium, Veterans Building*

Symposium on Hypertension

Medical Aspect S MARX WHITE, M D , Minneapolis

General Neurological Procedures ALFRED W ADSON, M D , Rochester, Minn

Neurological Treatment. MAX MINOR PEET, M D , Ann Arbor, Mich

*Wednesday, 8 15 p m—Auditorium, Veterans Building*

The Diagnosis and Treatment of Stone in the Common Duct ARTHUR W ALLEN, M D , Boston

Adrenal Cortical Tumors GEORGE F CAHILL, M D , New York

Fracture Oration Fundamentals versus Gadgets in the Treatment of Fractures PAUL B MAGNUSON, M D , Chicago

*Thursday, 8 15 p m—Auditorium, Veterans Building*

Ischemic Contractures ARTHUR STEINDLER, M D , Iowa City, Iowa

Cerebral Injuries Due to External Trauma GEORGE W SWIFT, M D , Seattle

The Diagnosis of Endometrial Hyperplasia LUCIUS E BURCH, M D , Nashville, Tenn

Treatment of Peptic Ulcer, Based on Physiological Principles ALTON OCHSNER, M D , New Orleans

*Convocation—Friday, 8 15 p m—War Memorial Opera House*

Invocation

Presentation of Candidates for Fellowship

Conferring of Fellowships The President

Conferring of Honorary Fellowships The President

Presidential Address DONALD C BALFOUR, M D , Rochester, Minn

Fellowship Address The Social Significance of Medicine ROBERT GORDON SPROUL, B S , LL D , Berkeley, Calif

## COMMITTEE ON ARRANGEMENTS

## EXECUTIVE COMMITTEE

HOWARD C. NASTFINGER, Chairman THOMAS F. MULLEN, Secretary

LEROY C. ABBOTT  
HAROLD BRUNY  
EDMUND BUTLER  
WHITFIELD CRANECHARLES A. DUKES  
LEO ELLINGER  
PHILIP K. GILMAN  
OLIVER D. HAMLENFRANK HOGMAN  
EMIL F. HOLMAN  
ALBION R. KILGORE  
FRANK W. LYNCHJOSEPH L. MCCOOL  
ISAAC W. THORNE

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## HOSPITAL REPRESENTATIVES

## SAN FRANCISCO—GENERAL SURGERY

Franklin Hospital—LEWIS GORDON, LEWIS BROOKS  
French Hospital—ASA COLLINS, EDWARD MORTENSON  
Hospital for Children—LEWIS ABBOTT, ALMA PETERSON

Letterman General Hospital—R. F. MEDICALS

Mary's Help Hospital—ISAAC THORNE, RAYMOND MILLER, EVERETT CARLSON, DUDLEY SMITH

Mount Zion Hospital—HAROLD BUTLER, FRANKLIN HAZEN, ALBERT L. BROWN

St. Francis Hospital—JAMES O'CONNOR, CALVIN A. WALKER

St. Joseph's Hospital—ALBION R. KILGORE, J. MINTON MERRIN

St. Luke's Hospital—G. D. DELPRAT, OTTO FRIEDLER

St. Mary's Hospital—THOMAS E. BAILEY, PHILIP ABBOTT, DANIEL SOBY

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Shriners' Hospital for Crippled Children—SYLVAN HAZEN  
Southern Pacific General Hospital—WILLIAM WARENBURG, FRANK R. GORDON

Stanford University Hospital—EMIL HOLMAN, PHILIP K. GILMAN, FREDERICK REEDER

Stanford University School of Medicine—LOREN CHAVELIER, EMIL REEDER

United States Marine Hospital—MARK J. WHITE, RICHARD L. W. DOR

University of California Hospital—HOWARD C. NASTFINGER, H. GLENN BELL

University of California Medical School—LAWLEY PORTER, WALLACE TERRY

Veterans Administration Hospital—P. E. JOHNSON, BENJAMIN H. HENNING, JOHN A. KENNEDY

## SAN FRANCISCO—SURGERY OF THE EYE, EAR, NOSE AND THROAT

French Hospital—EDWARD C. FARRIS, RAYMOND, VICTOR D'ENTRILLE

Hospital for Children—GEORGE HOGNER

Letterman General Hospital—A. E. SCHLAEGER, H. C. MATHWELL

Mary's Help Hospital—FRANK H. and J. W. CRAWFORD

Mount Zion Hospital—FRANK ROOTE, HERBERT COBY

St. Francis Hospital—CONSTANCE BRIDGES, AUBREY RAYMOND

St. Joseph's Hospital—ROY PARKINSON

St. Luke's Hospital—ANDREW E. DIXON, CHARLES BATES

St. Mary's Hospital—FRANK COVILAK, STANLEY BRIDGES

Southern Pacific General Hospital—WILSON SWETT

Stanford University Hospital—EDWARD REWELL, HAW BAKER, HARRINGTON GRABER, LOUIS MORTENSON

United States Marine Hospital—RA. ABBOTT

University of California Hospital—WALLACE SMITH, FRED C. CONDER, ROBERT C. MARTIN, C. ALLEN DICKET

Veterans Administration Hospital—J. J. CAYTON, OTTO BARRAN

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## PRELIMINARY CLINICAL PROGRAM

GENERAL SURGERY, GYNECOLOGY, OBSTETRICS, ORTHOPEDICS, UROLOGY,  
SURGICAL PATHOLOGY, ETC

## OPERATIVE CLINICS IN SAN FRANCISCO HOSPITALS—DAILY

## SAN FRANCISCO HOSPITAL

*University of California Service*

HAROLD BRUNN, GEORGE K. RHODES, A. R. KILGORE,  
C. L. CALLANDER, S. H. MENTZER, A. L. BROWN,  
H. W. STEPHENS, F. S. FOOTE, M. W. DEBENHAM,  
H. M. BLACKFIELD and L. GOLDMAN General surgery  
F. HINMAN, C. JOHNSON, S. OLSEN, L. PLAYER, J. J. SUL-  
LIVAN, W. A. CARROLL and T. O. POWELL. Urological  
operations  
W. G. MOORE, A. M. VOLLMER and M. SCHULZE. Gynec-  
ological operations  
H. W. FLEMING, H. A. BROWN and L. B. LAWRENCE  
Neurosurgical operations  
LEROY ABBOTT, F. G. LINDE, F. C. BOST, W. J. COX and  
K. O. HALDEMAN Orthopedic operations

*Stanford University Service*

LEO ELOESSER. Lobectomy for lung tumor, flap operation  
for tuberculous empyema, disarticulation at knee joint.  
W. L. ROGERS. Apicolysis (paraffin fill)  
J. M. MEHERIN. Gastric resection (Billroth I)  
EDMUND BUTLER. Pyloroplasty for peptic ulcer, atresia  
of colon, congenital  
J. CLINE. Exploration of biliary duct  
C. MATHEWSON. Open reduction of spiral fracture of the  
tibia, sequestrectomy for tuberculosis of the pelvis.  
D. KING. Nonunion of carpal scaphoid  
M. R. OTTINGER. Resection for carcinoma of the colon  
E. TOWNE. Laminectomy for decompression of cauda  
equina.  
E. MORRISSEY. Removal of cord tumor  
L. REYNOLDS. Cystectomy for carcinoma of the bladder  
G. HARTMAN. Suprapubic prostatectomy  
L. MICHAELSON. Plastic on kidney pelvis  
R. CRAIG. Nephrectomy  
K. SCHAUFF. Removal of fibromyoma of the uterus  
A. PETTIT. Vesicovaginal fistula.  
H. VON GELDERN. Perineal repair operation  
C. COOLEY. Operation for pelvic inflammatory disease  
R. DUNN. Hyam's coization of the cervix  
D. DALLAS. Vaginal hysterectomy

## UNIVERSITY OF CALIFORNIA HOSPITAL

HOWARD C. NAFFZIGER, D. JONES, JR., H. BROWN and R.  
AIRD. Neurosurgical operations.  
HAROLD BRUNN and H. STEPHENS. Thoracic surgery  
R. ABBOTT, F. BOST, K. HALDEMAN and W. KEYS. Ortho-  
pedic surgery  
FRANK W. LANCH, A. MAXWELL, M. SCHULZE, D. MOR-  
TON and C. HAYDEN. Gynecological and obstetrical  
operations  
FRANK HINMAN, C. JOHNSON, S. OLSEN and B. WAYMAN  
Urological operations.  
W. S. TERRY. General surgical operations, thyroidectomy  
H. SEARLS and H. GLENN BELL. Carcinoma of colon,  
cholecystectomy, popliteal aneurism  
C. ROSSEN. Appendectomy, hernioplasty  
M. S. WOLF. Carcinoma of rectum and lower bowel.  
F. FOOTE. Partial obstruction, new operations  
E. O. BARTLETT. Carcinoma of breast

## STANFORD UNIVERSITY HOSPITAL

EMMET RINFORD, EDMUND BUTLER, R. GILMAN, L. CHAND-  
LER, EMILE HOLMAN and S. BUNNELL. General ab-  
dominal surgery, gastro-intestinal surgery, hernias  
EMILE HOLMAN and LEO ELOESSER. Thoracic surgery  
F. REICHERT and E. TOWNE. Neurosurgical operations  
R. GILMAN, EMMET RINFORD and EMILE HOLMAN. Thy-  
roid, biliary tract, liver and pancreas surgery  
A. L. FISHER, D. KING and M. MENSOR. Orthopedic  
operations  
J. DILLON and L. REYNOLDS. Urological operations  
L. ENGE, H. A. STEPHENSON, C. FLEUHMANN, P. E. HOFF-  
MAN, G. CRAIG and W. STEVENS. Gynecological and  
obstetrical operations  
F. REICHERT and EMILE HOLMAN. Cardiac conditions,  
circulatory diseases  
C. B. PALMER and R. BURROWS. Injections, anesthesia  
R. A. SCARBOROUGH. Proctological operations  
A. DAVIS and S. BUNNELL. Plastic surgery, industrial  
cases, skin diseases.

## ST MARY'S HOSPITAL

T. E. BAILLY. Gastric surgery, gastrectomy  
RODNEY YOELL. Gall bladder surgery, cholecystectomy  
D. SOOY. Surgical intervention for duodenal ulcer  
C. P. MATHE. Nephropexy for nephroptosis  
E. TOPHAM. Inguinal hernia  
JUSTIN MCCARTHY. Industrial emergency cases  
EDMUND BUTLER. Surgery of the colon.  
GEORGE K. RHODES. Emergency surgery  
EDMUND MORRISSEY. Sympathectomy for Raynaud's dis-  
ease  
PHILIP AENOT. Obstetrical surgery  
T. GIBSON. Nephrectomy  
W. FAULKNER. Bronchoscopic diagnosis in cases of lung  
abscess  
J. LOUTZENHEISER. Orr treatment for delayed bony union

## LETTERMAN GENERAL HOSPITAL

R. F. METCALFE. Cauterization of cervix, penneorrhaphy,  
suspension of uterus, gastrojejunostomy, cholecystec-  
tomy, hemorrhoidectomy, colostomy for rectal car-  
cinoma, cesarean section  
F. L. COLE. Hernia, appendectomy, inguinal hernia,  
ventral hernia  
H. S. BLESSE. Genito-urinary operations, electrical re-  
section  
B. S. BURNET. Thoracotomy for empyema, orthopedic  
operations, bone graft, open reduction of tibia, ex-  
cision of cartilage, knee.  
P. E. DUGGINS. Curettage and insertion of Carsten pessary  
for sterility

## ST JOSEPH'S HOSPITAL

ALSON R. KILGORE, J. M. MEHERIN, F. SHEEHY and C. E.  
SMITH. General surgical operations.  
R. SOTO-HALL and K. HALDEMAN. Orthopedic operations  
E. MORRISSEY. Neurosurgical operations  
H. VON GELDERN. Gynecological operations  
T. GIBSON. Urological operations

## MOUNT ZION HOSPITAL

- HAROLD BEYER Total thyroidectomy for cardiac disease.  
 F. I. HARRIS Tumor operation for undescended testicle, first and second stage procedures, resection for lesions of descending colon, radical mastectomy Perty cavity and endocholeus.  
 A. L. BROWN Plastic repair of pendulous breasts, hernia surgery.  
 W. WALSHY Appendectomy.  
 M. GROSSER and A. WEISS Blood transfusion, citrate, Luedemann and Unger methods.  
 L. HOFFMAN Hysterectomy.  
 L. D. PIERCE, A. BRING and D. V. CHAMBERLAIN Radical calectomy, fracture of scapula.  
 H. BLACKFIELD Plastic correction of congenitally protruding ears.  
 HAROLD BEYER and A. L. BROWN Phrenic evulsion thoracoplasty.  
 A. ZONET and D. A. BROWN Electrocoagulation of tumors of the rectum hemorrhoidectomy under local infiltration.  
 L. C. JACOBSON Cancer of the urinary bladder transurethral prostatectomy.  
 H. A. R. KROTHMAN The problem of urinary lithiasis nephrectomy, pyelotomy, ureterectomy.  
 D. STALLON and M. POLAR Hydrocele operation, plastic operation for phleboma; cystoscopy.  
 A. KENTON Injection of vas deferens for chronic epididymitis.  
 R. K. BAKER Classical ovariotomy section.  
 A. BROWDER Demonstration of cervical repair immediately following delivery.  
 F. FRANK Muscle splitting extraperitoneal lumbar sympathectomy ganglionectomy new approach sacral sympathectomy posterior cervicodorsal sympathectomy ganglionectomy.  
 EDWARD H. BOLTE, HENRIET H. SCHULTZ and DR. LAZAR Demonstration of introduction of esophageal by vertebra, crystal, gas and oxygen, spinal.

## SOUTHERN PACIFIC HOSPITAL

- W. B. CONYER and J. D. HUNTER Superior cervical sympathectomy for angina pectoris, showing picture demonstration of actual color.  
 C. MATHEW and T. GIBSON Transurethral prostatectomy.  
 F. GREENWOOD Cholecystectomy.  
 F. R. DERRICK Inguinal hernia, ambulant treatment by injection.  
 C. WALKER and J. BOHR Open reduction of fracture.  
 OSCAR F. NOLAN and THOMAS E. GIBSON Suprapubic prostatectomy.  
 W. W. WASHINGTON Thyroid surgery.

## FRENCH HOSPITAL

- F. A. LOWE Fractured humerus, internal arrangements of knee joint.  
 O. W. PIERCE and O. O'CONNOR Removal of nasal bump.

## VETERANS ADMINISTRATION

- Staff Colly operation for carcinoma of the rectosigmoid, second stage, gastrectomy.

## ST LUKE'S HOSPITAL

- ALANSON WICKER, G. D. DELFRAT, PAUL CASTELLINI, A. H. ROSSIGNO, OTTO H. FRIEDBERG, DR. SULLIVAN, DR. MOORE and ALBERT M. VOLLMER General surgical operations.  
 GEORGE J. MCCORMICK, RUDOLPH L. DIEHL and DR. COX Orthopedic operations.  
 L. P. FLAYER, HENRY D. CHALL and MILEY B. WESSON Urological operations.  
 J. M. MONAGHAN Proctological operations.

## U. S. MARINE HOSPITAL

- ROBERT A. JONES Excision of pilonidal sinus and rectal operations, cholecystectomy and atropoplasty (Olsen tubular flap); Dupuytren's contracture.  
 RICHARD L. WALKER Inguinal hernioplasty using pedicled fascial strips, operation for scabies (Myrmecol); arthroscopy of the knee with excision of internal semilunar cartilage tumor operation (Fessenden) phrenic neurectomy.  
 FLETCHER C. STEWART Transurethral resection of prostate.

## FRANKLIN HOSPITAL

- K. OUELLE Gastro-intestinal surgery.  
 L. BRIDGES Abdominal operations.  
 J. SALK, V. LULLON, W. MONTGOMERY and W. COX, Inguinal surgery and orthopedics.  
 O. W. PIERCE and O. O'CONNOR Reconstruction surgery of head, face and neck after burns; repair of eyelids, correction of flexion contractures.

## MARY'S HELP HOSPITAL

- R. MILLERER Radical neck dissection.  
 E. CARLSON and C. C. MCCLURE Abdominal operations.  
 M. MASON and L. PARKER Orthopedic surgery.  
 M. VICKI Urological operations.  
 H. VON GELDER and A. SCHMIDT Gynecological and obstetrical operations.

## HOSPITAL FOR CHILDREN

- C. HOWE Thyroidectomy.  
 MORRIS E. EDWARDS Thyroglossal duct cyst.  
 ALMA FRYEDRICH Supravaginal hysterectomy total hysterectomy vaginal plastic.

## ST FRANCIS HOSPITAL

- O. B. O'CONNOR Plastic surgery Reconstruction of face after burns, rib cartilage transplant to the nose; removal of nasal bump cleft palate reconstruction surgery of the hand.  
 W. W. WASHINGTON Thyroidectomy.  
 L. K. REYNOLDS and O. NOLA Prostatectomy urethral transplants.

## SHELMER'S HOSPITAL

- SILVAN L. HAAS Longitudinal osteotomy transplantation of muscles in paralysis, stabilization of foot; fusions of spine, lengthening of leg, congenital dislocation of hip; Bone operation for obstetrical paralysis with transplantation of trapezoid; fusion of hip plastic operation.

## CLINICAL DEMONSTRATIONS IN SAN FRANCISCO HOSPITALS—DAILY

## GENERAL SURGERY

- A S WHITE and F I HARRIS Injection treatment of hernia  
 HAROLD BRUNN Appendicitis  
 S R SHEPARD Rupture of the spleen  
 J HOWLER WOOLSEY and H GLENN BELL Splenectomy  
 WALTER B COFFEY Inspection of an industrial medical and surgical center, ward rounds, demonstration of cases, postoperative treatment  
 EMERY RIXFORD Knotty problems in industrial surgery  
 Traumatic carcinoma of breast, ruptured heart, traumatic thrombosis of iliac and other large veins  
 EMILE HOLMAN Operative cure of recurrent and direct inguinal hernia  
 GEORGE K RHODIS Hematogenous perinephric abscess, peritonitis and drainage  
 M W DEBENTHAM Aseptic meningitis following spinal anesthesia  
 A L BROWN Pulmonary embolectomy, motion picture demonstration of the Trendelenburg operation on cadaver  
 H BRODIE STEPHENS Subphrenic abscess, vaccination of the pleural and abdominal cavities  
 WALTER BIRNBAUM Tendon repair, acute gonococcal tenosynovitis  
 ALSON R KILGORE, OTTO H PRILEGER and R S STONE Treatment of breast cancer, end results  
 OTTO H PRILEGER Soft tissue sarcomas  
 ALSON R KILGORE Cystic disease of the breast, cancer  
 C I CALLANDER Gas bacillus infection, new amputation of thigh in lower third, treatment of septic joints.  
 EDWARD BUTLER Emergency surgery  
 EDWARD BUTLER, I R REYNOLDS, L H GARLAND and J B McNAUGHT Old healed ruptured bladder, diagnostic difficulties and value of x ray in diagnosis, x ray in differential diagnosis of acute abdomen  
 EUGENE S KILGORE Circulatory disease in differential diagnosis of acute abdomen  
 CARLETON MATHISON, JR., and J B McNAUGHT Lymphogranuloma inguinale  
 A S MURPHY Postoperative infections  
 I W THORNE Squamous and basal cell carcinoma of face and neck, pathology, diagnosis and treatment  
 Z E BORN Biopsies and tumor surgery, mixed tumors of the parotid  
 EVERETT CARLSON Carotid body tumors, splenectomy, indications and technique  
 FRANK E STILES Treatment of varicose veins  
 J F RICKARD Intestinal obstruction

## SURGERY OF THE THYROID

- WILLIAM J KERR, HENRY H SEARIS, JANE T PAXSON and R S STONE Activities of the thyroid committee of the University of California Hospital with follow up studies after various lines of treatment  
 HENRY H SEARIS, E I BARTLETT and C L COVNER Chronic diffuse thyroiditis  
 HENRY H SEARIS and JANE T PAXSON Clinical picture of toxic adenoma with normal or lowered metabolic rate  
 WILLIAM J KERR The heart in hyperthyroidism  
 M L MONTGOMERY Lingual thyroid  
 THEODORE ALTHAUSEN Surgical implications of hepatic damage in thyrotoxicosis  
 R. J MILLNER Parathyroid damage during thyroidec-  
 tomy

## GENITO URINARY SURGERY

- FRANK HINMAN, CLARK M JOHNSON and BRENT WEYMAN Tumors of the testicle, pathology, demonstration of hormone tests, end results, uretero-intestinal anastomosis, experimental work, drawings and motion picture demonstration, demonstration of patients, prostatic, pathology, indications for different types of surgery, end results by different methods  
 C P MATHIE Surgery of the prostate  
 T F GIBSON Newer aspects of renal tuberculosis  
 L P FLAYER and H D CRALL Gracilis transplantation for urinary incontinence  
 MILLY B WESSON Conservative surgical treatment of nephrolithiasis  
 L C JACOBS Calculi of urinary bladder, suprapubic and transurethral prostatectomy  
 H A R KREUTZMANN Urinary lithiasis, nephrotomy, pyelotomy and nephrectomy  
 BERNARD STRAUSS and M L POISE Operation for hydrocele, plastic operation for phimosis  
 A F STIFFIN Injection of vas deferens for chronic epididymitis  
 J V FORD and GEORGE W HARTMAN Demonstration in urology  
 C P MATHIE and T F GIBSON Transurethral prostatectomy  
 T E GIBSON and O F VOLAN Suprapubic prostatectomy  
 J R DILLON Treatment of chronic pyelitis and pyelonephritis, treatment of cancer of prostate, technical improvements in surgical treatment of undescended testicle  
 W F STEVENS Unusual pathological conditions of the urinary tract in women  
 EDGAR POTTS A new aseptic technique for uretero-enterostomy, mechanism of ascending infection of the urinary tract, experimental observations  
 SIDNEY OLSEN Tuberculosis of the genito-urinary tract, urinary calculi  
 CLARK M JOHNSON Trauma of the genito-urinary tract, infections of the genito-urinary tract, renal and pararenal infections, renal anomalies  
 L P FLAYER Kidney lavage  
 W A CARROLL Ureteral lithiasis, rupture of kidney  
 T O POWELL Newer knowledge of tumors of the testicle with special reference to gonadotropic hormone excreted in the urine  
 M R OTTINGER, LLOYD R REYNOLDS and J B McNAUGHT Torsion operation for undescended testicle, torsion of testicle  
 GEORGE W HARTMAN Hematoma and pyuria, renal tuberculosis  
 W A SUMNER Relationship of chronic infections to lesions of the genito-urinary tract  
 LEWIS MICHELSON Obstruction of the neck of the bladder in the female  
 R GLENN CRAIG Ureteral pain of obscure origin  
 MORRELL VECKI Renal movability

## ENDOCRINOLOGY

- R F ESCAMILLA Consideration of abdominal pain of endocrine origin  
 SAMUEL CORN and F I HARRIS Discussion of the treatment of undescended testicle by operation and glandular extracts  
 LEO STANLEY Endocrinology in a penal institution.

## ORTHOTEDIC SURGERY

- GEORGE J. MCCARTHY, W. COX and R. L. DILLON. Fracture of neck of femur: treatment without external splinting.
- L. D. PRINCE, A. B. SERRY and D. D. CHANDLER. Fracture of os calcis; replacement of tibial shaft by fibula following osteomyelitis; treatment of borstus.
- R. L. WATSON. Clinical demonstration of Roger Anderson's Wright-O-Matic splint and abductor traction and contraction methods applicable to Thomas or Hodge's splints.
- LEROY C. ASHOTT. The shoulder joint.
- JOHN B. DE C. M. BATHURST. The shoulder joint.
- J. F. REICKARTER. Vitamin C deficiency in arthritis.
- KENNETH HALDEN and JOHN B. DE C. M. BATHURST. Demonstrations of bone growth.
- FRANCIS BAKER. Heat therapy.
- F. A. LOWE. Internal derangements of knee joint, etiology and motion picture demonstration, fracture of knee-joint, classic and motion picture demonstration.
- J. J. LOFTICROFT. Arthroplasty of foot.
- S. L. HALL. Application of Hibbs-Romer plaster for scoliosis, results of treatment for scoliosis, results of tendon transplantation, Legg-Perthes disease.
- J. J. HALL, W. O. MONTGOMERY, V. M. DILLON and W. J. COX. Industrial surgery and orthopedics.
- J. H. O'CONNOR. Reduction of complicated fractures, closed methods, demonstration of cases, indications for open reduction.
- C. A. WALKER. End results of open reduction of fractures: treatment of compression fractures of spine, eye cases; fractures of clavicle and patella.
- W. W. WALKER. Dislocations following fractures, factors influencing period of recovery.
- LEONARD W. LAY. Arthritis of the hip.
- D. KING. Functional anatomy and pathology of the shoulder joint.
- A. L. FLEWER. Treatment of flat feet.
- MERRILL C. MICHON. Osteogenic stimulus of space relation of bacteriophage to the Ott treatment of osteomyelitis.
- NELSON J. HOWARD. Traumatic lesions of bones, tendons and muscles.
- LEON PARKER. Femoral tendons in Pagen's disease.
- D. KING. Treatment of chronic sclerosing osteomyelitis.
- F. G. LYNN. Compression fractures of spine: new vision of fractures.
- F. C. BOST. Hibbs-Romer treatment of scoliosis: dislocation of carpal scaphoid: fracture of ankle, ligamentous tears of ankle: treatment of fracture of os calcis.
- W. J. COX. Internal derangement of knee joint, rupture of ligaments, treatment of fracture of femoral neck with Smith-Petersen saws.
- KENNETH O. HALDEN. Pathology of acute osteomyelitis, pathology of chronic infection of bone.
- RALPH SOTO-HALL and KENNETH O. HALDEN. Fracture dislocation of cervical spine: Dehner's fracture apparatus.
- PAUL E. JOHNSON, B. H. HERRING and JOHN A. KERRICK. Disability ratings of Veterans: Adaptation for orthopedic conditions of the extremities.
- CARLETON MATTHEWSON, JR. and J. B. MCNABNEY. Treatment of spiral fractures of tibia, open and closed methods of treatment of fractures of extracranial, tuberculous of pelvis.
- D. KING, J. M. MERRICK and R. A. SCARBOROUGH. Fracture of the carpal scaphoid: surgical approaches to bones and joints, the Ott method of treatment of osteomyelitis.

- NELSON J. HOWARD. Fractures of the upper end of the humerus, motion picture demonstration.
- MICHAEL C. MICHON and LEON PARKER. Unusual features of the spine: treatment of osteomyelitis with surgical biopsy.
- C. C. McRAE. Lesions of skull bones of the head.
- EDGAR L. GILBERT. Problems in treatment of fractures.

## SURGERY OF THE GASTRO-INTESTINAL TRACT

- HAROLD BRYCE. Cancer of rectum.
- F. I. HARRIS. Constricting (chronic) enteritis (regional ileitis): treatment of appendix stump, necroterectomy.
- FRED H. KERRY. Common complications of peptic ulcer.
- E. J. BART, F. H. KERRY, THOMAS ALTRACH and RALPH RABINOWITZ. Postoperative care of intestinal conditions.
- M. F. COYNE. Primary duodenitis and results of ulcer cases, types of operation, causes of recurrence.
- LEON GOLDMAN and THOMAS ALTRACH. Perforation of peptic ulcer.
- J. HOWARD WOODRUFF and H. GUY. Bell. Carcinoma of stomach.
- M. L. MONTGOMERY and JOSEPH M. SWIFT. Acute intestinal obstruction, experimental and clinical.
- H. GUY. Bell. Sebaceous intestinal obstruction, local and type (chronic constricting enteritis).
- H. GUY. Bell and LEON GOLDMAN. Congenital lesions, tumors, diverticula of small bowel.
- M. S. WOOD. LEON GOLDMAN and H. GUY. Bell. Carcinoma of large bowel.
- DESMOND SMITH and J. W. MORGAN. Carcinoma of rectum.
- ASA W. COLLINS. Pyloroduodenal and gastro-enterostomy.
- LEROY BRYCE. Diagnosis and treatment of intestinal obstruction.
- F. K. BRYCE. Peptic ulcer: indications for surgical treatment.
- R. W. WALKER. Acute perforation of peptic ulcer: complications and end-results in 100 cases.
- EMERY GIBBLE. Radical surgery for gastric and duodenal ulcers, diverticula of colon, closure of colostomy: preservation of anal sphincter.
- J. A. OULFORD. Chronic appendicitis, end-results of operation.
- J. E. BOEN. Mortality rate of operations for appendicitis.
- R. A. SCARBOROUGH. Developments in surgical treatment of carcinoma of rectum, 200 cases.
- EMERY HOGAN. Causes for failure to control symptoms and to prevent gastrointestinal vici in gastric surgery.
- GOTTFRID W. NAGEL, F. L. REICHERT and MARY E. MAYER. Chronic regional enteritis, clinical, experimental.
- DAVID A. WOOD. Multiple primary carcinomas of colon complicating multiple polyps of colon.
- NELSON J. HOWARD. Acute granuloma of large bowel.
- HAROLD BRYCE. Carcinoma of large bowel, carcinoma of rectum, bowel obstruction.
- GEORGE K. RICHARDS. Spontaneous perforation of caecum from obstruction in distal colon.
- DANIEL SCOTT. Choice of operation in gastric surgery.
- EDWARD TOWMAN. End results in surgery for gastric ulcer.
- H. F. HILL, GEORGE BARNETT, J. M. MERRICK, J. W. CLINE and A. C. McKEENE. Lesions of the upper gastro-intestinal tract: anatomic infections of liver and gastro-intestinal tract.
- DESMOND SMITH. Operation for rectal fistula and hemorrhoidectomy: motion picture demonstration.
- ASA W. COLLINS. Operations on the stomach, particularly pyloroduodenal and gastro-enterostomy.

## THORACIC SURGERY

- HAROLD BRUNN, A. L. BROWN, H. KOSFENBLUM and J. J. SIMPSON Symposium on surgery of the heart with particular reference to adhesive pericarditis
- LEO LLOES-LEF, PHILIP H. PIERSON, W. I. ROGERS, W. G. BURKHARD, DAVID A. WOOD, W. K. CLARK and I. H. GARLAND Various types of bronchial stenosis, mycotic infections of the lung, tumors of the lung, empyema
- EMIL HOLMAN Technical improvements in partial selective thoracoplasty, resection of transverse process, resection of scapula, ligation of the pulmonary artery as a therapeutic measure in pulmonary hemorrhage, carcinoma of lung simulating inflammatory disease
- HAROLD BRUNN, SIDNEY J. SHIPMAN, H. BRODIE STEPHENS, A. L. BROWN, M. W. DUFFINHAM and A. GOLDMAN Lung suppurations, empyema, artificial pneumothorax, phrenic avulsion, thoracoplasty
- ALAN SON WEEKS and G. D. DELFRAT Thoracoplasty
- RAY KISTLER Diaphragmatic hernia
- SIDNEY J. SHIPMAN Pneumothorax in pneumonia
- W. B. TALLNER, JR. Bronchiectasis, treatment of chest injuries
- A. L. BROWN Collapse therapy in pulmonary tuberculosis
- S. SNEFMAN Lymphoblastoma of mediastinum
- C. A. WALKER Phrenicectomy for pleuropneumothorax and adhesions
- A. GOLDMAN Staphylococcal infections of the lung, chemotherapy in tuberculosis
- T. F. MULLEN Antithoracic esophagoplasty
- MARY E. MATHIES Experimental study of the effect of various pathological conditions upon the dual blood supply of the lungs
- EDGAR POTTS A simple apparatus for tidal and siphon irrigation and its application in treatment of empyema
- DAVID A. WOOD and MARY E. MATHIES Exhibit of clinical and experimental observations on the dual blood supply of the lungs in various pathological states
- LYOYD B. CROW Pulmonary infarct

## GYNECOLOGY AND OBSTETRICS

- WILLIAM G. MOORE Endometriosis, fibromyomata of uterus
- A. M. VOLLMER Rubin's insufflation test, trichomonas vaginalis
- R. K. SMITH Classical cesarean section, motion picture demonstration
- FRANK LAMCH, ALICE MAXWELL and R. S. STONE Uterine cancer, follow up, X ray therapy, radium therapy
- MARGARET SCHULZE Special ovarian tumors
- A. H. HEALD and ALICE MAXWELL X ray pelvimetry, direct method
- PHILIP H. ARNOT Conduct of labor in posterior position
- LUDWIG ENGEL Dysmenorrhea, causes and treatment, sterility, diagnosis and treatment
- C. F. FLUHMANN, P. F. HOFFMAN and GERTLUDE F. JONES Endocrinological aspects of gynecology, modern methods of diagnosis, blood and urine hormone tests, biopsy of endometrium, hormone therapy
- A. V. PETTIT Results of hyperpyrexia in treatment of acute and chronic pelvic inflammatory disease
- LUDWIG ENGEL Radiation therapy of carcinoma of cervix, methods and end results
- A. M. VOLLMER Treatment of abortions
- MARGARET SCHULZE Multiple pregnancies, pyelitis with pregnancy, hydatidiform mole and chorio-epithelioma, cardiac disease with pregnancy
- KARL L. SCHAUFF Fibromyoma of the uterus
- HANS VON GELNERN Plastic operations on pelvis
- C. L. COOLEY Demonstration of gynecological cases
- R. D. DUNN Treatment of incomplete abortions

- D. A. DALLAS Operations in obstetrics
- BEVERLY SIMPSON Separated placenta
- ADOLPH I. SCHMIDT Uterine bleeding

## SURGERY OF THE BILIARY TRACT, LIVER AND PANCREAS

- ALAN SON WEEKS and G. D. DELFRAT Common duct stone, hydatid disease of liver, granuloma inguinale
- F. I. HARRIS Acute cholecystitis
- CARL HOAG Reconstruction of common duct
- H. CLARK SHEPARDSON and HANS FISHER Pancreatic dysfunction, hypoglycemia
- H. GLEN BELL and THORODOR ALTHAUSSEN Operative mortality and pre-operative management of cholecystitis, glucose therapy, Rose Bengal and other tests
- IRVING H. KRIESE and THORODOR ALTHAUSSEN Medical and surgical jaundice, cirrhosis of liver, differential diagnosis from carcinoma of stomach
- JESSE I. CAMP and FREDERICK S. FOOTE Experimental work in human jaundice
- KARL SCHMIDT The bile salts
- EMIL HOLMAN Postoperative and inflammatory stenosis of the bile passages
- M. W. DUFFINHAM and J. M. SWINERT Liver abscess
- STANLEY H. MENTZER Acute cholecystitis, obstructive cholecystitis
- ROBERT A. YORLL Gall bladder anomalies
- T. I. MULLEN Recurrence of symptoms after surgery

## CIRCULATORY DISORDERS

- M. I. MONTGOMERY Therapeutic venous occlusion
- C. A. NOBLE, JR. Postoperative cardiac versus circulatory collapse

## NEUROSURGERY

- HOWARD C. NAZZIFER Late results in the treatment of malignant exophthalmos, brain tumors, factors in influencing recovery after peripheral nerve injury, cervical ribs, "scalenus syndrome without cervical ribs"
- HOWARD W. FLEMING Subdural hematomata, cerebrospinal rhinorrhea, relief of intractable pain, cranial approach for orbital tumors, cranio-cerebral injuries
- EDMUND MORRISSEY Neurologic clinic on lesions of the cauda equina, diagnosis and treatment of subdural hemorrhage, diagnosis of subdural hemorrhage
- O. W. JONES, JR. Spinal cord tumors
- H. A. BROWN Low back injuries, spinal cord injuries
- F. B. TOWNE Treatment of acute head injuries
- I. I. REICHERT Neuralgias of cranial nerves, demonstration of patient and lantern slides
- ROBERT AIRD Encephalography, clinical, experimental, intradural alcohol injections for intractable pain
- L. B. TOWNE, E. MORRISSEY, J. W. WOLFSON and D. WOOD Surgical lesions of the spinal cord, dynamics of epilepsy
- I. B. LAWRENCE Spinal cord tumors, tumors of cauda equina
- LEE HAND Regeneration of peripheral nerves of hand
- EDMUND J. MORRISSEY Diagnosis and treatment of subdural hemorrhages

## SURGERY OF INFECTIONS

- A. S. WHITE Treatment of staphylococcus infections with staphloid
- S. A. GOLDMAN Studies on staphylococcus infections
- F. J. MCCARTHY End results in infections of the hand
- B. F. ALDEN Relation of focal infection to Wassermann fast lues
- V. H. MITCHELL Treatment of anaerobic infection of the extremities presentation of cured patients



## CLINICS IN ALAMEDA COUNTY HOSPITALS—WEDNESDAY

## ALAMEDA COUNTY HOSPITAL

- WHELFIELD CHASE and W. EARL MITCHELL—9. Carcinoma of stomach  
 F. A. H. BOWLER and THEODORE LAWSON—9. Carcinoma of rectum  
 H. W. HARRIS and DOT D. WEAVER—11. Carcinoma of colon  
 LEONARD P. ALLEN—12. Carcinoma of breast  
 SCHMIDT EYERHOLM—9. Extraperitoneal thoracoplasty: intrapleural pneumothorax; clinic on phrenic intervention and thoracoplasty. Discussion by CHESTER BONE  
 WARREN B. ALLEN—12. Neurosurgery  
 W. F. HOLCOMB—9. Arthroplasty of hip  
 L. B. BARNARD—10. Arthroplasty of shoulder  
 E. N. EWER—9. Total hysterectomy; subtotal hysterectomy; discussion of electrical service at Alameda County Hospital  
 CLARENCE A. DUFFY—11. Gynecological cancer clinic. Demonstration of intrapleural alcohol effusions and presentation of cases  
 ALBERT M. MEADE, LEON KIRKALL, JOHN A. DAWSON, T. L. BUCKLEY and associates—9. Personal prostatictomy, suprapubic prostatectomy, transurethral prostatectomy. Operations, demonstration of cases and discussion

## Dry Clinics, 8—11:30

- CHARLES A. DUFFY and associates. Cancer clinic  
 HAROLD H. JENCKOCK, N. A. CARY and associates. Traumatic and orthopedic clinic, demonstration of Swenson cast dryer, Bell table, plaster models, splints, etc.  
 W. H. SARGENT and C. B. BOWEN. X-ray exhibit and discussion  
 GEORGE MOORE. Pathological exhibit and conference

## BERKELEY GENERAL HOSPITAL

## Dry Clinics, 9—12

- FRANK D. WALKER. Cholecystitis, observations and comments on surgical treatment  
 CLAUDE H. GIBSON. Ectopic pregnancy recurring on same side  
 WILLIAM W. CROSBY. Polycystic kidney; nephrectomy; prostatic management  
 J. F. CARLSON. Osteochondroma with involving all epiphyses in one extremity. Clinico-pathologic  
 W. H. RICE. Parathyroid disease. Gross specimens and microprojections  
 R. O. V. NEWS. X-ray demonstration and discussion

## CHILDREN'S HOSPITAL

- ROY NELSON—9. Demonstration of methods of treatment of esophageal stricture due to lye  
 W. W. CROSBY—9. Postmortem findings in the kidneys of children, lantern slide demonstration  
 CLIFFORD BAKER—9. Clinic on undescended testis. Demonstration of postoperative results. Discussion of the effect of anesthesia. 3. demonstration of operation

## ALTA BATES HOSPITAL

- Staff—9. Operations and dry clinics

## SAMUEL MERRITT HOSPITAL

- WARREN B. ALLEN—9. Reconstruction of skull defects, operation and demonstration of cases  
 W. F. HOLCOMB and D. D. TUFFENHAR—9. Orthopedic operations and demonstrations  
 MARK L. KUTNER—9. Rectal surgery and presentation of cases  
 FRANK H. BOWLER—9. Thyroidectomy  
 W. H. SARGENT—9. X-ray demonstration and discussion of cases  
 ROBERT A. CLARK—9. Pathological exhibit; demonstration of frozen section techniques and specimens  
 WHELFIELD CHASE—9:30. Pyptic ulcer. Judd pyloroplasty  
 W. EARL MITCHELL—10:30. Pelvic tumor  
 HERBERT EVANS—11. 30. Cholecystectomy  
 CHARLES A. DUFFY—11. Apicalysis, operation. demonstration of thoracic chest. Discussion by HAROLD THORPE  
 H. N. ROWELL, A. M. SMITH, W. H. STEINMAN, A. A. ALLEN, W. B. KIRBY, STEWART V. LEWIS, H. GORDON MACLEAM, FLETCHER B. TAYLOR, VICTOR G. ALLEN and HOWARD ROBERTS—11. Symposium on pre- and postoperative care. Management of surgical jaundice and stomach cancer, diabetes in surgery; traumatic and postoperative pancreatitis, cardiac and renal complications, postoperative psychosis. Library in relation to abdominal surgery. Discussion and demonstration of cases

## PERALTA HOSPITAL

- J. L. LOVIE—9. Cholecystectomy  
 EMIL A. MAYOR—9. Carcinoma of breast, radical removal  
 F. M. LOVIE and JOHN W. SERRA—9. Pilon cystitis  
 CHARLES W. FOWLER—9. Orthopedic treatment of epiphyseal lesions, correction of upper extremity involvement in poliomyelitis  
 H. J. THOMPSON and J. LOVIE—11. Electric desiccation in cutaneous malignancies  
 JOHN W. SERRA—10. Vaginal plastic  
 T. FLOYD BELL—9. Pelvic tumor  
 T. C. LAWSON—11. Hernia, fascial repair  
 F. N. JACOBSON—11. Bladder surgery  
 PAUL MICHAEL—9 to 11. Pathological demonstration and exhibit  
 J. D. COATES—9 to 11. X-ray demonstration and exhibit

## COWELL MEMORIAL HOSPITAL

- HERBERT EVANS, ROBERT LAWSON, C. A. KORY and associates—9. Exhibit and discussion of latest advances in radiology, inspection of laboratories and hospital with special reference to the systematic medical care of emergency students, discussion of laboratory technique with particular reference to anesthesia

## ALAMEDA SANATORIUM

- J. ORANTZOFF—9. Hernioplasty under local anesthesia  
 G. R. BAKER—9. Cholecystectomy  
 CLAYTON HALL—10. Resection of stomach

## PROVIDENCE HOSPITAL

- O D HAMLIN—9 Intestinal anastomosis.  
 J RADFORD FEARN—9 Vaginal hysterectomy under local anesthesia.  
 A REIS—10 Cholecystectomy, new method  
 THEODORE M WELLER—10. Cesarean section  
 N AUSTIN CARY—11 Sacro-iliac fusion  
 PHILIP J DICK—11 Posterior gastro-enterostomy  
 MICHAEL TORRANO—12 Herniotomy under local anesthesia  
 S A JELTE—9 to 12 X-ray demonstration and discussion

## EAST OAKLAND HOSPITAL

- DON D WEAVER—9 Ulcer of the stomach.  
 O R ETTER—9 Surgery in the diabetic patient, dry clinic.  
 R G VAN NUYS—10. Dry clinic Visceroptosis and position of the viscera in healthy young adults, X-ray demonstration  
 BROOKS STEPHENS—10 30 Hallux valgus  
 CLARE RASOR—10 30 Prolapse of uterus  
 ALEXANDER H GRIFFITH—11 Carcinoma of the recto-sigmoidal junction, Lahey technique.

## SURGERY OF THE EYE, EAR, NOSE, AND THROAT

## CLINICS IN SAN FRANCISCO HOSPITALS—DAILY

## UNIVERSITY OF CALIFORNIA HOSPITAL

## Tuesday

- JOSEPH L MCCOOL, FREDERICK C CORDES, JOSEPH W CRAWFORD, C ALLEN DICKEY and DAVID O HARRINGTON—9 Ophthalmological operations  
 R. C MARTIN and FREDERICK C CORDES—9 Toti Mosher operation.  
 WALLACE SMITH, LOUIS MORRISON and EDITH STOKER—9 Otolaryngological operations

## Dry Clinics—2

- FREDERICK C CORDES Surgery of traumatic cataracts  
 J W CRAWFORD Tuberculosis of the eye  
 C ALLEN DICKEY Surgery of the vertical muscles  
 DAVID HARRINGTON Contact glasses, practical demonstration.  
 R. C MARTIN and STERLING BUNNELL. Injuries and repair of the facial nerve

## Thursday

- JOSEPH L MCCOOL, FREDERICK C CORDES, JOSEPH W CRAWFORD, C ALLEN DICKEY and DAVID O HARRINGTON—9 Ophthalmological operations  
 R C MARTIN and FREDERICK C CORDES—9 Toti Mosher operation.  
 WALLACE SMITH, LOUIS MORRISON and EDITH STOKER—9 Otolaryngological operations

## Dry Clinics—2

- JOHN SAUNDERS Regional anatomy of the mastoid and pathways of infection of the intracranium.  
 HOWARD C NAFFZIGER. Brain abscess arising from middle ear and mastoid infections  
 WALLACE SMITH Phlebitis and thrombosis following middle ear and mastoid infections

## Friday—2

- FREDERICK C CORDES Surgery of complicated cataracts.  
 J W CRAWFORD The eye in diabetes  
 C ALLEN DICKEY The value of orthoptic treatment.  
 DAVID HARRINGTON Tobacco amblyopia and its treatment.

## ST MARY'S HOSPITAL

## Thursday—2

- FRANCIS CONLAN, STANLEY BURNS and FRANK HAND Treatment of posterior sinusitis. Blood dyscrasias in relation to the ear, nose and throat Treatment of bilateral abductor paralysis.  
 FRANK HAND Radical antrum

## HOSPITAL FOR CHILDREN

## Thursday—2

- GEORGE N HOSFORD and AVERY M HICKS Technique for the determination of the hydrogen ion concentration of tears The significance of pH of tears in ocular symptoms and treatment. Indications for and results of orthoptic training Relation of vertical imbalance of extra-ocular muscles to gastric symptoms, posture, temperament and aptitude for school work and occupation Congenital muscle palsy Motion picture demonstration of O'Connor technique for heterophoria and heterotropia

## Days to Be Announced

- GEORGE N HOSFORD and AVERY M HICKS—9 Extraction of congenital cataract, muscle operations, O'Connor cinch shortening for simple exotropia, simple esotropia, vertical deviations, muscle transplants for external rectus palsy, superior rectus for paralysis of the superior oblique (Jackson's technique), Mota's operation for congenital ptosis, Toti Mosher operation for occlusion of nasolacrimal duct (with Drs Martin and Hosmer)

## SAN FRANCISCO HOSPITAL

## Tuesday—2

- WARREN D HORNER. External indectomy, history, uses, technique and advantages  
 C ALLEN DICKEY and J W CRAWFORD Safety procedures in cataract operations, akinesis, intra-orbital injections, lid sutures, pre-operative medication.  
 WARREN D HORNER, C ALLEN DICKEY and J W CRAWFORD The use of synthetic epinephrin bitartrate in ocular therapeutics  
 AUBREY RAWLINS Osteoma of the antrum, some curious foreign bodies in the lungs, cases of recovery from otitic meningitis, extensive osteomyelitis of the frontal bone  
 HARRINGTON B GRAHAM. Foreign bodies in the lungs, stenosis of the esophagus, cancer of the larynx  
 HARRINGTON B GRAHAM and J M WOLFSOHN Extensive abscess of the meninges  
 RAE ASHLEY Treatment of tuberculosis of the larynx

## STANFORD UNIVERSITY SCHOOL OF MEDICINE

## Wednesday—2

- FRANK RODIN Congenital and hereditary eye defects  
 AVERY HICKS Ocular torticollis  
 D FISCHER Retinal detachment, methods and results.

## MOUNT ZION HOSPITAL

## Tuesday

HERBERT J. COHEN, EDWARD LIMPET and JOHN SRAFF—  
Tonsil operations, local and general anesthesia, dis-  
section, bladder stone

## Wednesday

HERBERT J. COHEN, EDWARD LIMPET and JOHN SRAFF  
Symposium on mastoidectomy  
GEORGE S. LACHMAN—Treatment of ocular albinism  
CHARLES WISE—Recently developed concepts in im-  
munology and bacteriology of value to the ophthal-  
mologist  
FRANK H. ROUTH—Treatment of acute rhidocyclitis  
G. Y. RYCE—Pathological demonstration of various eye  
conditions

## Thursday

Staff—  
Nasal operations. Submucous resection, electro-  
coagulation of turbinates, sinus surgery

## Days to Be Announced

FRANK H. ROUTH and GEORGE S. LACHMAN—  
Ophthalmological operations. Cataract, strabismus, plastic on  
eyelids

## SOUTHERN PACIFIC HOSPITAL

## Thursday

WILSON F. SHERK and JOHN C. WILLIAMS—Cases and  
demonstration of cases

## CLINICS IN ALAMEDA COUNTY HOSPITALS—WEDNESDAY

## PROVIDENCE HOSPITAL

A. J. HOWELL—  
Reconstruction of nose  
ROBERT O'CONNOR—  
Muscle shortening, cataract  
Cataract operation  
GEORGE McCLELL and NELSON KEELER—  
Ear, nose  
and throat surgery  
RICHARD BRANTFORTH—  
Metal operation  
ROY NELSON—  
Esophagoscopy and bronchoscopy  
BROCK STEPHENS, J. —  
Cataract operation  
FRANK BAXTER—  
Ear, nose and throat operations  
MILTON H. BOUTER—  
Ear, nose and throat operations  
ALEXANDER GALLERSTEIN—  
Ear, nose and throat oper-  
ations  
W. A. MAGRATH—  
Eye operations  
ALVIN P. WOLD—  
Eye surgery  
F. C. KRACAW—  
Ear, nose and throat surgery

## LETTERMAN GENERAL HOSPITAL

## Tuesday

A. E. SCHLAEMER and HERBERT H. PRICE—  
Tonsillectomies, adenoidectomies, general anesthesia  
HARVEY C. MAXWELL—  
Eye surgery, general anes-  
thetia. Strabismus correction by O'Connor tendon  
crotch and by Janssen recession

## Wednesday

A. E. SCHLAEMER—  
Tonsillectomies, local anesthesia  
nasal operations, local anesthesia

## Thursday

HARVEY C. MAXWELL—  
Eye operations, local anesthe-  
sia. Cataract extraction, pterygium transplant, strab-  
ismus correction

## Friday

A. E. SCHLAEMER, HERBERT H. PRICE and HARVEY C.  
MAXWELL—  
Sinus surgery local anesthesia, extra-  
nasal radical frontal rhinopharyngotomy radical  
maxillary sinusotomy; bronchoscopy, esophagoscopy

## ST. LUKE'S HOSPITAL

## Tuesday and Thursday

JOSEPH L. MCCOOL, C. ALLEN DICKY, A. E. ROBERTSON  
and CHARLES BATES—  
Ophthalmological clinic

## VETERANS ADMINISTRATION

Staff—  
Bronchoscopic examinations

## Dry Clinic 2-4 30 p. m.

Staff—  
Discussion of operative procedures, demonstration  
of cases, lectures and motion picture demonstration

## ALAMEDA SANATORIUM

B. M. STEPHENS—  
Cataract

## CHILDREN'S HOSPITAL

M. E. LARSON—  
Strabismus, operative treatment



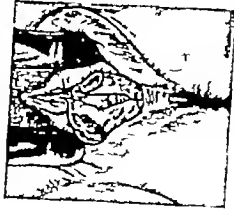


Fig. 1 Early hypertrophic stage.



Fig. 2 Second stage, moderate atrophic changes.



Fig. 3 Third stage, advanced trophy.

*Chronic (trophic) Dermatitis filio 1 uba — Fred L. Allen and Edward M. Davis.*

# SURGERY, GYNECOLOGY AND OBSTETRICS

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## CHRONIC ATROPHIC DERMATITIS OF THE VULVA<sup>1</sup>

IRRED I. ADAIR, M.D., F.A.C.S., AND M. J. EDWARD DAVIS, M.D., F.A.C.S., CHICAGO, ILLINOIS

**U**NDER this broad descriptive terminology we wish to describe a condition the nomenclature of which has aroused considerable discussion. It was first described under the term of "kraurosis vulvæ" by Breisky in 1885 and each succeeding author has been so dissatisfied with this limited descriptive term as to introduce a new one. Thus we have an array of names for this condition, the more common of which are leucoplasia (Morris), leucoplacic vulvitis (Taussig), leucokraurosis (Graves), and pruritus vulvæ. Although the catchy term "kraurosis" will probably remain attached to this condition, we suggest the use of a broader, more descriptive name—chronic atrophic dermatitis of the vulva. This simplified nomenclature is in line with the general tendency to use simple descriptive terms. Furthermore, this term is broad enough to include early cases of derma-

titis of the vulva which may develop into typical kraurosis.

KRAUROSIS, LEUCOPLACIC VULVITIS, LEUCOKRAUROSIS

These three most common terms are all used specifically by a few authors, but interchangeably by most of them to designate progressive pathological atrophic changes in the vulva. Undoubtedly, different patients present themselves with various pictures of this condition. However, we agree with Taussig and Graves that these various clinical manifestations represent different stages of a progressive disease which, if allowed to go untreated, will ultimately develop leucoplasia and possibly carcinoma. It is, therefore, perhaps simpler to think of the entire condition under the broad name of chronic atrophic dermatitis of the vulva, reserving kraurosis and leucoplasia for various stages of the condition.

### INCIDENCE

The disease is very infrequent and cases are rarely seen in general practice. In large gynecological clinics, however, a fair number are encountered. In 9,682 gynecological patients examined for the first time at the University of Chicago Clinics, chronic atrophic dermatitis of the vulva was encountered in 23 patients—an incidence of 0.24 per cent. Probably many cases seen in their incipency, when pruritus is the only symptom, remain unrecog-

Fig. 1 Photograph showing the early hypertrophic stage. Note the marked edema of the labia minora and majora and the presence of superficial blebs and petechial hemorrhages. There is slight involvement of the perineum.

Fig. 2 Photograph showing the second stage. Atrophic changes can be noted in the disappearing labia minora and narrowing of the introitus. The clitoris is entirely covered over by the adherent atrophic preputial folds. Note the characteristic whitening of the mucosa and the numerous superficial petechial hemorrhages. Note likewise the sharply demarcated involvement of the lesion.

Fig. 3 Photograph showing the third stage. All signs of elasticity have disappeared and the vaginal orifice is greatly constricted and rigid. The labia minora have disappeared completely, only the urethral orifice and the preputial folds being present. The perineum is involved in a typical triangular shape.

<sup>1</sup>From the Department of Obstetrics and Gynecology, The University of Chicago, and The Chicago Lying-in Hospital. Read before the Chicago Gynecological Society, October 26, 1934.

nized until the pathological condition becomes well marked. The number of cases recorded in the literature is not a true index of its frequency.

#### ETIOLOGY

Chronic atrophic dermatitis of the vulva is distinctly a disease of the menopausal or post-menopausal years. It rarely involves young women during their active sex years. Parity apparently plays no rôle as the incidence is probably as frequent in women who have had children as in nulliparous women. Cessation or waning of the ovarian function undoubtedly is an important factor in this condition. The average age in Taussig's large series of cases was 49 years and that in our group was 52 years. The condition occasionally occurs in young women particularly those suffering from abnormalities of ovarian function. These cases however are rare and when they do occur they merit careful study as to the etiology. Of the patients in this group 7 still had regular or irregular menses, and 10 had ceased menstruating.

Inflammation is probably the most important, constant etiological agent in the production of this condition. A fertile field for inflammation is provided in the physiological atrophic changes which occur during or after the menopause as is pointed out by Sedz, Veit, Taussig, Graves, and Smith all emphasize the inflammatory process associated with this condition. Pruritus is a constant symptom in this condition, and several of the authors look upon it as an etiological agent in the production of the disease. It is hardly fair to assume that it is the only factor because there must always be some cause for the pruritus. The constant itching leads to trauma in the form of many small wounds and bruises which heal slowly and with difficulty because of the infection and the continued irritation. In the slow healing process a piling up of the superficial layer of epithelium occurs. This may account for the keratosis and whitening of the superficial epithelium giving the characteristic picture of leukoplakic vulvitis.

#### PHYSIOLOGICAL ATROPHY OF THE VULVA

Normally following the onset of the menopause a slowly progressive atrophy of the sex

organs takes place. This is most marked in the uterus and the ovaries and less marked in the vagina and the external genitalia. During the early years of the menopause this atrophy of the external genitalia may be barely visible becoming more marked with advancing age. The atrophy consists in a shriveling up of the labia minora and majora and the vagina. This shriveling up process is aided by the loss of fat in these parts. The skin may become smooth thin and glistening and the vaginal introitus may become greatly narrowed. The vagina, likewise undergoes even more extensive atrophic changes, which we have studied recently. The trauma of intercourse examination or any simple manipulation may cause these atrophic areas to become bruised or cracked thereby producing petechial hemorrhages which may lead to soreness or itching. So far these changes may all be considered entirely physiological as the result of a loss of certain ovarian function. This condition has been called simple kraurosis because of the characteristic shriveling up process, but it is far better to ascribe it to the end results of the cessation of certain physiological ovarian activity.

A sudden cessation of ovarian activity resulting from an artificial menopause induced by radiation or surgical castration may hasten the development of the physiological atrophy of the vulva.

As a rule this physiological process requires no treatment as it produces no symptoms. However when it occurs in a middle aged woman particularly one in whom an artificial menopause has been induced the narrowing of the introitus may make coitus difficult exceedingly painful, or even impossible. It may be necessary to provide additional room at the introitus by some surgical expedient such as the operation devised for a vaginismus.

When this physiological atrophy is marked and repeated trauma causes fissuring, bruising and petechial hemorrhages, it is possible for these bruised and fissured areas to become infected. The atrophic skin is no longer a good barrier to the introduction of even the usual variety of organisms which are always present and the infection may become more or less chronic. Trauma petechial hemor-

rhages, and infection cause irritation of the superficial nerve endings. This irritation is usually interpreted by the patient as itching which is mild at first and becomes more marked as the condition progresses. Itching calls for scratching on the part of the patient, thereby causing more bruises and trauma to the delicate vulval structures. Thus, in a period of months or years, a true chronic atrophic dermatitis of the vulva develops, predisposed by a normal physiological process.

Three or four stages of the disease are usually described, however, the process is progressive and no clear-cut picture of each stage can be seen. They rather tend to merge into one another until the well developed atrophy appears. Various stages coincide and may be seen at the same time.

*First stage* In the earliest stage, the inflammatory process may be most marked. The entire vulva is swollen, red, bruised, and painful. The labia minora and majora and preputial folds stand out prominently due to the swelling. In some cases the edema may be so marked as actually to cause small superficial blebs of the labia minora and majora. The skin appears stretched, glistening, and at times almost parchment-like in its transparency. Superficial wounds, abrasions, and petechiae may also be present. The condition involves the labia majora and minora and the introitus, ending at the mucocutaneous junction and the perineum (Fig. 1). If the infection is marked the inflammatory process may extend out laterally over the skin of the thigh, causing fissures in the groin. Burning and itching are marked and the skin is actually painful to the touch or the pressure of clothing. This early stage may last for weeks, months, or years, depending on the acuteness of the process and the amount of discomfort to the patient. If the inflammation is marked, the usual soothing treatment of the skin will cause the process to subside somewhat.

*Second stage* The atrophy begins to manifest itself grossly in the second stage. The skin itself appears thickened, indurated and leathery in character due to increasing thickness of the keratin layer. It has lost its elasticity and the usual suppleness, so that an ordinary pelvic examination in a multiparous

woman causes pain. The color is a whitish to a mottled gray, with scattered pinkish or reddish areas caused by the petechial hemorrhages. These superficial hemorrhages in their absorption and organization go through the various stages of the usual subcutaneous hemorrhage, providing the various colorations to the vulva. The labial folds flatten out so that they may appear only as ridges. All trace of the labia minora may disappear. The preputial folds likewise flatten out or become completely obliterated (Fig. 2).

The characteristic distribution of this condition is most interesting. The changes are usually limited to the non-hairy portion of the vulva and are sharply demarcated at the mucocutaneous junction with the vagina. The perineal skin is usually likewise involved, extending down to the anal region. Occasionally, the atrophic process extends about the anus posteriorly to it. This specific limited area of the diseased process lends credence to the endocrine origin of the condition.

*Third stage* After a period of years most cases are finally characterized by this last stage, during which many of the patients present themselves for treatment. The skin over the involved area becomes smooth, glistening, semitranslucent and parchment-like. Minor trauma causes it to crack, fissure, and bleed. It is pearly-white or bluish-white in color, with petechial hemorrhages in the various stages of absorption. All signs of elasticity have disappeared. The vaginal orifice becomes greatly constricted and rigid. The labia minora have completely disappeared. The preputial folds have become ironed out and only the urethral orifice stands out anteriorly. The extent of the perineal involvement varies in different patients. Here the skin assumes an appearance typical of the vulvar changes. This stage of the disease, likewise, is progressive, although it may appear unchanged for several years at a time. There does not seem to be a complete spontaneous retrogression of this condition, although there may be long periods during which the symptoms as well as the course may remain quiescent (Fig. 3).

Leucoplasic areas often develop in chronic atrophic dermatitis as single or multiple discrete plaques involving the inner surface of





Fig 4 Photomicrograph of the hypertrophic stage showing the increased thickness of the superficial layer of keratinocytes and marked elongation of the papillae. There are no abnormal changes in the basal layer of cells, but beneath it there is marked edema and characteristic layer of inflammatory cells. X45.

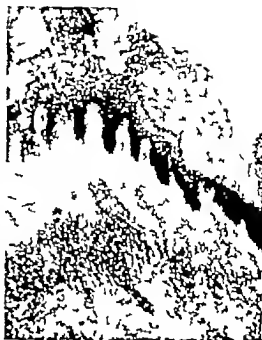


Fig 4A Photomicrograph showing the characteristic changes in the hypertrophic stage. X90.

the labia majora and minora, the area over the perineum or around the clitoris. The latter is most frequently involved. These leucoplasic areas may cause the most intense itching. They are grayish or bluish in color with a definite thickening of the skin or mucous membrane. Fissures or ulcerations may occur about these regions.

There are rare cases in which the changes described are confined to one side of the vulva or remain localized to such an extent that one may speak of a localized leucoplacia. However in the large majority of patients, this condition symmetrically involves the entire vulva and extends into the perineum.

#### HISTOPATHOLOGY

In the histological picture of this condition one may easily follow the progress of the dis-

ease. Few specimens have been taken in the incipient state because surgery has been rarely resorted to until the condition is far advanced. It is possible, however, to recognize two distinct stages—the hypertrophic and the atrophic stages. Tauszig, however, has pointed out correctly that in one specimen all stages of the disease may be found. Thus the progressive atrophy does not continue at an equal pace over the entire area.

In the early *hypertrophic stage* after the acute inflammation and edema have partially disappeared one finds marked elongation of the papillae and an increased thickening of the superficial layer of keratinocytes (Figs 4 and 4A). The basal layer of cells shows no abnormal changes. All of the cells stain deeply and show marked granulation of the cytoplasm. This granulation gives the same appearance to these cells as is normally found in the intra-epithelial zone of cornification or Dierck's layer seen in the vaginal epithelium (Fig 5). Normally this layer becomes most marked in the vaginal mucosa just about the



Fig 5 Photomicrograph of the hypertrophic stage showing a layer of large cells filled with granules between the basalis and functionalis. This layer resembles the intra-epithelial zone of cornification or Dierck's layer seen in the vagina.  $\times 300$



Fig 6 Photomicrograph of atrophic stage showing the relationship between basalis and greatly thickened functionalis. Note layer of large cells containing granules of various sizes beneath these two layers. The basal layer of cells appears frayed and irregular.  $\times 170$

time of ovulation. Apparently it is associated with the building up of the functionalis. The keratin layer increases considerably in thickness. The most marked changes are found just beneath the squamous epithelium. There is a marked cellular infiltration of the connective tissue consisting of inflammatory cells. Round cells predominate, although polymorphonuclear leucocytes, plasma cells, and other wandering cells may be seen. These inflammatory cells occur in smaller and larger foci and at times densely infiltrate the sub-squamous zone. Increased vascularity and edema are likewise noted. Marked changes occur in the elastic fibers early in the disease. They may be entirely absent between the papillae.

In the late *atrophic stage* the squamous epithelium has become greatly decreased in thickness. In some areas it consists of only four or five layers of cells. The papillary pro-

jections have almost disappeared. The basement layer of cells appears ragged, irregular in outline, and stains poorly. In the individual cells, liquefaction necrosis may be seen. The superficial keratin layer has steadily increased so that it now appears as thick or thicker than the basalis (Fig 6).

The most interesting changes may be seen in the dermis beneath the squamous epithelium, where there are large edematous areas in which few, if any living cells may be found (Fig 7). These may be due to a transudate of serum and a liquefaction of the connective tissue of this layer. As a result of the edema the elastic tissue has become separated from the epidermis and now appears frayed and irregular beneath this edematous area. In places the elastic tissue fibers seem to be swept up into irregular bundles like driftwood. It is likely that they have lost their continuity, ruptured, and retracted to form



Fig 7 Photomicrograph showing marked trophy of the basalis. Beneath this layer there is extensive edema in which there remains small strands of cells composed of leucocytes, plasma and mast cells. There is marked absence of elastic tissue in this edematous zone. This elastic tissue appears beneath the basal layer.  $\times 95$



Fig 8 Photomicrograph of section stained with Hagerst and Götsch's elastic tissue stain. The edematous layer beneath the basalis shows almost complete absence of cells. Beneath this layer there appear fragmented strands of elastic tissue stained black and swept together like driftwood in this irregular zone.  $\times 55$

these unusual accumulations (Fig 8). The zone of inflammatory cells is now present beneath the edematous layer consisting chiefly of mononuclear and polymorphonuclear leucocytes and mast cells. All of the wandering cells may be seen. In the dermis is a marked absence of sebaceous glands of all types. Fewer blood vessels than appear in the hypertrophic stage may be seen. There is relatively little change in the deep layers of the cutis and the subcutaneous tissue except for some atrophy.

Histologically leucoplasic areas represent hypertrophic processes and may be indistinguishable from kraurosis vulvae. There is a marked hyperkeratosis, the elastic tissue is frayed and broken up and a diffuse infiltration of inflammatory cells occurs, consisting chiefly of lymphocytes which are perivascular in distribution. The small vessels in the sub-epithelial layer show varying degrees of narrowing due to thickening and fibrosis of their walls. Again we wish to call attention to the fact

that the atrophic and hypertrophic stages may be found in the same specimen. Thus, this progressive process does not involve all parts with equal rapidity.

#### SYMPTOMS

Pruritus with rare exceptions, is a predominant symptom, and was the chief complaint of all the patients in this group. The duration of pruritus may be noted in the tabulation of these cases. The itching may be slight at first, causing little inconvenience. It steadily becomes worse so as to upset the normal nervous equilibrium of the patient. The itching may be worse at night leading to marked loss of sleep (Tables I and II).

In a few instances, burning rather than itching is the most common complaint. This is most marked during the acute stage of the disease, particularly when the element of infection predominates. If there is marked excoriation about the vulva burning on urination may be troublesome. Likewise if the

TABLE I

Present age Menopausal	Symptoms	Areas involved	Treatment			Results
			X-ray (Total Roentgen unit)	Medical	Surgical	
41 45	Genital itching— burning—year	Labia minora majora perineum, anus	816 Aug. 1933	Calamine lotion	Vulvectomy May 1933	No 51928 Results of vulvectomy good Other therapy gave no relief Slight itching of anus still persists
41 44	Vulval anal itching, burning 10 years	Vulva and perineum	1000 Jan. 1933	Lotus Salt packs	Vulvectomy June 1933	No 60588 Results of vulvectomy good Other therapy gave no relief Stage 1
48 4	Vulval itching years	Labia minora majora perineum vulva	None	Calamine Phen I lotion	Vulvectomy Apr. 1933	No 60535 Local therapy gave no relief Partial vulvectomy itching has returned Stages 2 and 3
49 40	Vulval itching burning after X-ray for carcinoma of cervix	Labia minora majora perineum vulva	None	Calamine lotion	Vulvectomy Apr. 1933	No 60001 Results of vulvectomy good Stages 1 and 2
46	Vulval itching, burning 3 months	Entire vulva perineum	138 Sept. 1930	Local therapy	Vulvectomy July 1931	No 60231 Felt fine 1½ years following radiation itching returned Results of vulvectomy excellent Stage 1
6 4	Vulval itching— burning months	Labia minora majora perineum vulva	11456 Nov. 1930	Local therapy	Vulvectomy Mar. 1931	No 60550 Radiation gave no relief Results of vulvectomy excellent Stage 3
40 44	Vulval itching 10 months Pea sized wart on labium 1 month (carcinoma of vulva)	Left labia entire vulva perineum	523 June 1933 After operation	Lotion	Vulvectomy May 1933	No 81533 No relief from local therapy Results of vulvectomy good
40 —	Vulval itching discharge 9 years	Labia minora majora perineum vulva	1035 May 1933	Local therapy	Vulvectomy Sept. 1933	No 50755 Symptom aggravated following radiation Results of vulvectomy excellent Stage 3
5 51	Genital itching— Severe irritation	Marked inflammation of parts extending to thighs & fema	Elsewhere	Amnionin	Vulvectomy Sept. 1933	No 10319 Radiation given elsewhere Amnionin therapy gave no relief Patient hospitalized for treatment of infection and vulvectomy Stage 1

excoriation extends to the anus painful defecation is the result. Many of these patients complain of dyspareunia and pain on examination. This is due to loss of elasticity of the skin causing cracking and fissuring.

The progress of the disease is slow. Mild cases may persist for years without causing great discomfort. The intolerable itching eventually brings the patient to a physician. In some cases the progress is more rapid so that in the course of a few months marked atrophic changes develop. The usual anti-pruritic lotions and ointments give little if any relief.

#### DIAGNOSIS

The vulva should be examined under subdued or indirect light which will accentuate the outline and appearance of the involved tissue. A well developed case of chronic atrophic dermatitis of the vulva should not be difficult to diagnose. It occurs particularly

in women at the menopause or postmenopausal period, thereby ruling out conditions causing pruritus in young women. On careful inspection the characteristic skin changes previously described will be noted and found to be well demarcated. In the early stages however, considerable difficulty in making a diagnosis may be encountered. At times a positive diagnosis may not be made until evident atrophy occurs and typical kraurotic and leucoplacic changes are manifest. In the early stage therefore all conditions which may engender itching of the vulva and the perineum should be ruled out.

Infections of the vulva cause pruritus. The various pyogenic organisms may be associated with leucorrhea and inflammation. The vestibule, labia minora and majora, and perineum may be reddened and tender. Smear and culture examinations will identify the various pyogenic organisms. Therapy directed

TABLE II

Percent age frequency	Symptoms	Areas involved	Treatment		Remarks
			X ray (Total & local)	Medical	
77	Severe itching, redness, swelling of vulva ears	Labia minora, clitoris, perineum, urethra	Fluor barium	Local therapy	No report. First treatment gave no relief. No clinic treatment.
47 46	Itching of perineum ears	Labia minora, clitoris, vulva	300 May 1911	Cocaine ointment	No report. Cocaine gave temporary relief. Scalp.
64 46	Itching of vulva to ears	Labia minora, clitoris, vulva	300 July 1910	Local therapy	No report. Radiation gave temporary relief. No report. Cocaine (at least did not return). Scalp.
98 46	Itching of vagina to ears	Labia minora, clitoris, vulva, perineum	300 Sept 1911	Local therapy	No report. Cocaine improved. Patient did not return. Scalp.
57 46	Itching of urethra 8 years	Labia minora, clitoris, vulva, perineum Extending into anal area	300 Mar 1911	Local therapy	No report. Marked relief for several months, but symptoms have returned recently. Scalp.
98 —	Itching of labia 5 years	Perineum extensively involved	300 Mar 1911	Local therapy	No report. Radiation gave relief for months, but symptoms gradually returned. Cocaine and fluor barium. Patient did not return. Scalp.
37 47	Severe itching of vagina, urethra 10 years	Labia minora, clitoris, perineum, vulva	None	Cocaine bismuth phenol	No report. Medical therapy gave temporary relief. Increased vulvar activity. Patient did not return.
45 —	Itching of labia minora ears	Marked edema of vulva, perineum	300 Jan 1911	Local therapy	No report. Cocaine therapy gave no relief. Cocaine fluor barium. Patient did not return. Scalp and
55 —	Itching of vulva	Labia minora, clitoris, vulva, perineum	None	Local therapy	No report. Local therapy gave no relief. Cocaine fluor barium. Patient did not return. Scalp.
98 —	Itching, burning of vulva, discharge, pain years	Labia minora, clitoris, vulva, perineum	None	Local therapy	No report. No treatment given. Cocaine and fluor barium. Patient did not return. Scalp and
66 55	Itching of vulva, pain, discharge, dysuria	Vulva, perineum	None	Anesthetics	No report. Improved under anesthetic therapy. Scalp.
98 55	Itching, discharge 4 months — years	Labia minora, clitoris, perineum, vulva	300 Sept 1911	Local therapy	No report. Radiation made condition worse. No cocaine. Cocaine to be done. Scalp.
98 —	Itching, discharge 4 months — years	Labia minora, clitoris, perineum, vulva	Fluor barium	Anesthetics	No report. Local treatment being given. An anesthetic therapy made condition worse. Expecting Scalp.
19 —	Itching of perineum — years	Labia minora, vulva	None	Itchy of condition	No report. Improved after medical treatment.

toward the eradication of the infection will result in a prompt improvement.

*Yeast infection* of the vulva is probably more common than is the consensus of opinion. It has been shown recently that it is almost always associated with diabetes. Superficial scrapings of the involved skin will show the organisms on microscopic or culture examination. Blood sugar determinations should be made in every case of vulvitis. Similar lesions elsewhere on the body may assist in making a diagnosis (Fig. 9).

*Other fungous infections* of the vulva may occur usually associated with lesions in the groins. The characteristic skin lesion is usually present. Microscopic examination will reveal the fungus as the etiological agent.

*Parasites* such as pediculi or pinworms occasionally are responsible for pruritus vulvae. In the absence of a specific skin lesion, other than the abrasions and trauma of scratching, careful examination of the vulval hair and the anal region should be made to determine whether or not parasites are present.

*Neurodermatitis.* Dermatologists recently have emphasized the importance of neurodermatitis as a cause for pruritus vulvae and ani. The occurrence of the condition in young women with an absence of any characteristic local changes in the skin should suggest a neurogenic origin. The presence of a neurodermite elsewhere substantiates the diagnosis. This condition is usually found in the nervous, unstable individual.



Fig. 9. Yeast infection of the vulva involving the labia skin, and both groins. Superficial skin scrapings revealed the organism on microscopic and culture examinations.

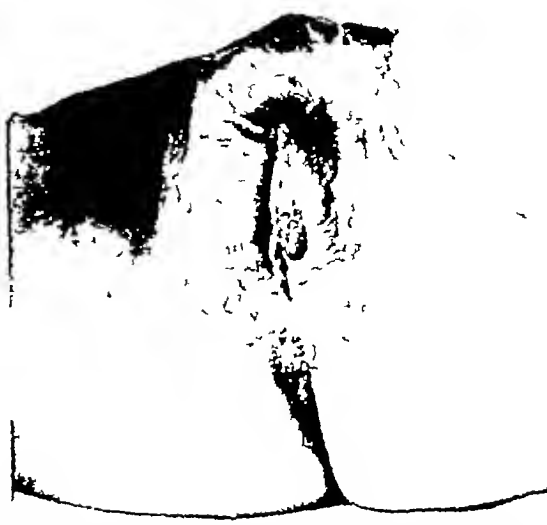


Fig. 10. Photograph of a small polypoid squamous cell carcinoma of 6 to 8 weeks' duration superimposed on chronic atrophic dermatitis of the vulva.

*Syphilis* has been given as an etiological agent for kraurosis vulva by the older authors. It probably has no relation to this condition. However, a Wassermann test should be made on every patient.

Many other rare conditions may be responsible for pruritus of the vulva and should be considered in the differential diagnosis.

The development of an *epithelioma* of the vulva is always a possibility and may occur at any stage in the disease. Every patient should be followed carefully and a biopsy made of any suspicious lesion. The appearance of a nodule on the vulva in a case of chronic atrophic dermatitis is highly suggestive of a squamous cell carcinoma, inasmuch as over 50 per cent of these patients ultimately develop malignant changes. Chronic atrophic dermatitis of the vulva is the most important so-called "precancerous lesion."

#### PROGNOSIS

The disease does not tend to regress spontaneously, although long periods may elapse during which there is little noteworthy change. The great danger to the patient is the possible development of a squamous cell carcinoma. Kraurosis and leucoplacic vulvitis predispose

to malignant changes in at least 50 per cent of the cases. Chronic atrophic dermatitis of the vulva may be termed a precancerous lesion for in no other condition is a disease so often followed by malignancy. It may arise in the hypertrophic or atrophic stages (Fig. 10).



Fig. 11. Photograph showing the postoperative results of a vulvectomy performed 2 years previously. On examination the vagina easily admits the finger. The patient has had no return of her symptoms.

## TREATMENT

Although many types of therapy have been advocated from time to time, surgery is the treatment of choice. In dealing with a lesion which is progressive in character and frequently followed by malignant changes, adequate surgical removal appears logical. A vulvectomy varying in extent with the area of the skin involved, removes all source of danger of malignancy. The operation carries with it very little risk and may be performed on almost any individual. We have done a number of vulvectomies under local anesthesia, supplemented by narcotics, with entire comfort to the patient. The relief from the pruritus is immediate. Convalescence is usually uneventful. Healing will generally occur by primary union if there is no constriction of the tissues. In middle aged women a functional vagina may be restored although in older women the normal vaginal atrophy precludes this (Fig 11). Tausig reports a case of leucoplasic vulvitis in a young woman who gave birth to a normal full term child following a vulvectomy.

X ray therapy has been given for this condition with some success. Early in the disease, before marked atrophic changes appear, radiation occasionally will give temporary relief from the pruritus. It does, however, recur and the progress of the disease continues unabated. Most of our patients received radiation therapy with little or no relief and were subsequently operated upon. Radium is not useful in the treatment of this condition.

The usual anti pruritic lotions, salves and ointments are of no benefit to allay the intolerable itching. Their efficacy is lost after several applications and the patient loses faith in their dispenser.

Hormonal therapy has been given with no apparent success. Future treatment along this line may eventually prove useful.

Leamouth has advocated sectioning the pudendal, perineal and other nerves of the vulva to allay the itching in chronic atrophic dermatitis. The results of this method have not been uniformly successful. In removing the itching, the patient may be lulled into a sense of security while malignant changes are

developing. The desirability of this form of therapy is open to question.

## CONCLUSIONS

1. The present terminology—kraurosis, leucoplasic vulvitis, leukokraurosis, etc.—is confusing and unsatisfactory as it describes only certain phases of this condition. It leads to failure in making a diagnosis of the early stages of the disease prior to the development of the shrinkage of kraurosis or the white areas of leucoplacia. Chronic atrophic dermatitis of the vulva is a simple and descriptive term for the entire process in its various manifestations.

2. In a period of 5 years we have encountered 23 patients with typical chronic atrophic dermatitis of the vulva—an incidence of 0.24 per cent. Vulvectomy was done in 9 patients with uniformly good results. Various types of treatment were given, including radiation in the majority of the patients, with only temporary relief.

3. The disease is progressive and does not tend to regress spontaneously although there may be periods of quiescence.

4. Surgical removal of the involved tissue is the only safe, logical and effective treatment in alleviating the symptoms and arresting the progress of the disease.

5. The condition is to be regarded as a precancerous lesion, with an incidence of carcinoma in over 50 per cent of the cases.

6. Vulvectomy is further justified as a prophylactic measure against carcinoma of the vulva.

## REFERENCES

- BREITZ: Ueber Kraurosis Vulvae, eine wenig beachtete Form von Elephantiasis an Perineum und Scheide. *Zentralblatt Med.* 86, 60.  
 GRAVES, W. P. and BREITZ, G. V. *S. J. Am. M. Ass.* 930, 92, 244.  
 LEAMOUTH, J. R. MONTGOMERY, H. and COUGHLIN, L. B. *Arch. Surg.* 933, 30, 90.  
 SEITZ, H. Ueber leukoplakische Veränderungen der Vulva ohne Beziehung zur Kraurosis derselben selbst zwei Fällen von Vulvocarcinom. *Blattsch. f. Geburtsh. Gynäk.* 903, 7, 1020.  
 TACSONI, F. *J. Am. J. Obst. & Gynec.* 930, 1, 42.  
*Idem*: Atrophic Diseases of the Vag. *Curtis' Obstetrics and Gynecology* Vol. 2, p. 63. Philadelphia W. B. Saunders Co. 931.  
 VERR, J. Kraurosis Vulvae (Leukoplakia Vulvae). *Handbuch der Gynäkologie* 9. ed. 94, p. 6.

## PHLEBITIS, THROMBOSIS, AND THROMBOPHLEBITIS OF THE LOWER EXTREMITIES<sup>1</sup>

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**P**HLEBITIS, thrombosis, and thrombophlebitis are discussed together here because it is difficult to draw a sharp differentiation between the three conditions. Most phlebitides are associated with some thrombosis and even the blandest thromboses provoke a reactive inflammation of the adjacent vein wall. The three terms moreover, are widely interchanged, usage frequently reflecting the opinion held as to the relative importance of vein infection and thrombosis in the evolution of the picture. Thus, in the German literature, the term thrombosis is widely encountered, thrombophlebitis being reserved for the frankly infective forms of the disease. In France, on the other hand, where the teachings of Vaquez still prevail, phlebitis is the term most often employed. It is the purpose of this paper to discuss briefly the conditions characterized by vein inflammation and thrombosis under a single heading, in the hope that some of the vagueness and confusion surrounding them may be dissipated.

### GENERAL CONSIDERATIONS

*Thrombosis* Three chief classes of causes for thrombosis have long been recognized. These are changes in the vessel wall, slowing of the circulation, and alterations in the composition of the blood itself. The last named of the three probably represents the oldest theory. John Hunter enunciated the belief that inflammation of the vein wall was the necessary precursor of thrombus formation, and that the clot was always secondary. Virchow established the conception of thrombosis as an intravascular coagulation due to slowing and eddying of the circulation. If the inflammation played any part, it was merely that of slowing the blood stream, thereby permitting the clot to form. Zahn, some 20 years later, demonstrated that trauma to the intima of living vessels resulted in local thrombosis. He observed the deposition of white blood cells along the injured surface and

differentiated between red and white thrombi, that is between coagulation of the blood as occurs in extravasated or completely stagnant blood, and agglutination, which is the primary process in intravascular thrombosis. Hayem and Bizzozero recognized blood platelets as independent blood elements, and demonstrated that it was their rôle, rather than that of the white corpuscles, in the agglutinative process, which initiated thrombus formation. Further studies by Eberth and Schimmelbusch, Welch, Aschoff, and others have confirmed these observations, and have added materially to our knowledge of the mechanism of thrombus formation.

Although their relative significance is still widely disputed, it is now generally accepted that all three of the factors mentioned are involved, and that an interaction of two or more is probably necessary for the development of thrombosis in the majority of cases. In the thrombophlebitides due to penetrating injuries, or arising by extension in areas of suppuration, the inflammatory alterations of the vein wall are obviously the initial changes. Bland thromboses, on the other hand, arising after clean operations or deliveries, and involving vessels at a distance from the field of operation cannot so easily be explained on the same basis. Between these two extremes are the large number of phlebitides with thrombosis arising during the course of infectious states, following operation or in the puerperium, in which the possibilities of infection somewhere in the body are present, but in which there is no direct connection between its location and the site of the phlebitis. In these cases, it is difficult to state whether the vein becomes infected first, with secondary thrombosis, or whether secondary infection of a thrombus occurs, with subsequent involvement of the vein wall.

Slowing of the circulation is certainly one of the important causes in the development of thrombosis. This is attested by the relative

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infrequency of thrombosis in the aorta and larger arteries despite the most extensive sclerotic changes, even to calcification and ulceration of the vessel wall whereas thrombosis of the veins is comparatively common. Postoperative thrombosis is practically never seen in children and is rare in young adults. It becomes frequent during middle and advancing age, when changes in the heart and blood vessels permit slowing of the blood stream. The vessels most often affected in this type of thrombosis are the large veins of the lower extremities, those of the left side being much more frequently involved than those on the right. In spite of the greater frequency of surgical intervention in the right half of the abdomen. This selective localization has been accounted for on the basis of anatomical variations on the two sides, such as greater length and obliquity of the left common iliac vein, pressure of the right common iliac artery which crosses and compresses it against the vertebral column, constriction in the arterial loop formed by the left internal and external iliac arteries (Kistler), and pressure from the adjacent portion of the colon all of which further favor local venous stasis. The frequent formation of thrombi in varicose veins, aneurysms and similar locations where slowing and eddying of the circulation occur further indicates the importance of this factor in the development of thrombosis.

Hunter showed, about a century ago that complete stagnation of the circulation by means of aseptic and traumatic isolation of a column of blood between two ligatures does not lead to thrombosis. This experiment has been confirmed many times, notably by Vaquer and by Baumgarten, and has been invoked as an argument against stasis being the sole cause of thrombosis. The invalidity of this argument lies in the failure to differentiate between thrombosis and coagulation. Coagulation such as occurs postmortem or when blood has been shed, is a function of stagnant blood and depends upon the liberation of ferments from the cellular elements, which activate the thrombin in the plasma. This, in turn, converts the soluble fibrinogen into strands of insoluble fibrin. The formed elements are enmeshed in the fibrin network

the whole solidifying into a more or less homogeneous jelly like mass. Thrombosis, on the other hand is a phenomenon of blood which is flowing albeit at a reduced rate and consists of the agglutination of platelets along the vessel wall to form a homogeneous layer. Superimposed upon this mass is a settling out of white blood corpuscles. This gradual building up of a white thrombus can occur only while the blood is still flowing. Fibrin formation plays no part in this picture except as a secondary process when as a result of the liberation of ferments from the agglutinated platelets and leucocytes, coagulation may occur at the periphery of the thrombus. As a matter of fact, thrombosis has been observed in blood rendered incoagulable by the addition of hirudin in the experience of Zurbelle. He cites similar experiments with hirudin which were carried out by Schwalbe and by Loeb, and with peptone by Eberth and Schummelbusch.

It is obvious, nevertheless, that slowing of the circulation is not the only factor involved in thrombus formation. Local trauma or inflammation of the vein wall, as was shown experimentally by Zahn and others and as is seen clinically following injury or suppuration will also lead to thrombosis at the site of vascular damage. This is the principle made use of in the artificial obliteration of varicose veins by means of injections of sclerosing substances. Intimal changes may well be a factor too in the spontaneous thromboses of varicose veins. However the demonstration of gross venous lesions accompanying the bland forms of thrombosis of the larger vessels is very rare. Furthermore the selective involvement of the left side is difficult to explain on the basis of primary pathological changes in the vein wall. In this connection it is interesting to note that Kristenson has recently described adhesions and fold formations in the intima of a large percentage of adult iliac veins studied at autopsy. These changes are sharply localized to the left common iliac vein. He believes that they are due to pressure from the iliac artery and considers them etologically significant in the development of thromboses. Similar changes have been described by Macfarrieh and others. Nevertheless, it still remains to

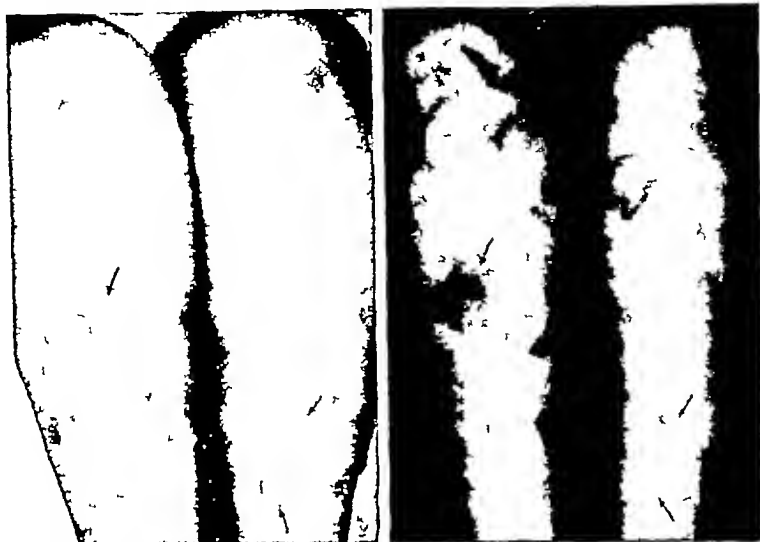


Fig 1 Relation of varicose eczema to varicosities Left, Patches of eczema in upper and middle portions of legs Right, Infra red photograph of same view, reveals varices directly beneath each patch of eczema

be proved that such lesions of the vein wall underlie thromboses in general

Changes in the composition of the blood which are frequently described as favoring the development of thrombosis are dehydration, increased viscosity, changes in the acid base reaction, greater fragility of the red cells, accelerated sedimentation rate, increased number and fragility of the platelets and shortening of the coagulation time These changes are frequently emphasized by clinical observers but their significance has not been definitely established The red and white corpuscles seem to play no part in the genesis of thrombosis Changes in these structures would, therefore, seem to have little bearing on the subject Increase in the number of platelets is often emphasized, but it is difficult to see how this finding alone could significantly determine thrombus formation Increased friability of the platelets alterations in their electrical charge, and greater tendency toward agglutination have also been mentioned and might be more directly related These are changes however which cannot readily be measured Thrombosis is frequently attributed to augmentation of the clotting factors and shortening of the coagulation time As

was stated before, these elements play no rôle in the initiation of the thrombus However they may affect the secondary, coagulative phase, and as such, play a rôle in the propagation of the peripheral portions of the thrombus

*Phlebitis* The inflammation of the vein which invariably occurs in the conditions under discussion varies widely in its source nature, intensity, and significance As is seen in the accompanying tables the range extends from simple, non-bacterial reparative inflammation following bland thrombosis to actual suppuration

The reparative inflammation secondary to bland and aseptic thrombosis represents the mildest grade of phlebitis It is often so slight as to be clinically unrecognizable, and the presence of the underlying thrombosis is consequently often not recognized Because of

TABLE I—ORIGIN OF VEIN INFLAMMATIONS

- 1 Reparative reaction to bland thrombosis
- 2 Metastatic infections
  - A Spontaneous phlebitis
    - a Normal veins
    - b Varicose veins
    - c Buerger's disease
    - d Phlebitis migrans
  - B Postoperative or puerperal phlebitis
- 3 Extension of infection by contiguity
- 4 Direct injury or infection

the mildness of the reaction provoked thrombi of this type are but loosely attached to the vein wall and readily break loose to form emboli. As will be shown later the sudden massive pulmonary emboli usually arise from this type of thrombus.

In most of the phlebitides, the organisms or toxins reach the affected vein by the metastatic route. They may come in direct contact with the intima of the vessel, or may lodge in the *vasa vasorum* as minute infectious emboli. Aschoff is of the opinion that in this form of thrombophlebitis too thrombosis is the primary process, and that circulating organisms are passively included in the developing thrombus. Bacterial growth within the thrombus may then lead to secondary infection of the adjacent portion of the vein wall. Metastatic infection accounts for the spontaneous thrombophlebitides of normal and varicose veins and probably for the vein inflammations of Buerger's disease and of phlebitis migrans. The postoperative and puerperal phlebitides arising at a distance from the field of infection or operation also fall within this category.

Mention should also be made of the remarkable tendency of veins to harbor latent infections for long periods of time. Repeated attacks of inflammation in the same or adjacent segments of vein are frequently due to periodic activation of the same infection rather than to new infections. This is particularly true of the subacute and chronic forms of phlebitis involving normal and varicose superficial veins and probably also of so called phlebitis migrans. De Takats has written of latent infections in varicose veins and Kendall and Jacques in unpublished observations, have obtained bacterial growth from a large proportion of specimens of vein removed during ligation of the long saphenous vein in cases of extensive varicosities. The ascending phlebitis which sometimes follows the injection of varicose veins is probably due to the activation of a pre-existent latent infection.

A third possible avenue of infection to the vein wall is by extension from suppurative processes about its radicles and progression by contiguity along the vein wall or along a thrombus forming within the vein. This type of infection may conceivably arise from an in-

fected placental site and lead to a suppurative thrombophlebitis, by extension of the iliac veins. A similar mechanism may explain the portal thromboses secondary to suppurative appendicitis. This method of infection however accounts for but a small fraction of the cases of phlebitis, and is particularly infrequent as a source of the phlebitides of the lower extremities.

A final type of phlebitis is that which arises by direct trauma to the vein wall as from a penetrating injury or perforation by a fractured bone spicule. In the same category are direct infections of the vein arising in suppurative lesions surrounding it and extending from the adventitia inward toward the intima. A classical example of vein infection by this mechanism is sinus thrombosis complicating mastoid suppurations. In the lower extremity phlebitis of this type may develop secondary to infected wounds, osteomyelitis, or pelvic abscesses overlying the large veins. This group too comprises but a small number of the vein inflammations, and the source of the infection is usually obvious. In these there can be little doubt that the thrombosis, if it develops at all is secondary to the initial lesion.

*Postoperative vein complications.* The thromboses and phlebitides arising as complications of operation or delivery are of particularly poignant interest to the surgeon. We may therefore summarize those changes in the organism brought about by these procedures which are conducive to the development of vein disease. Retardation of the circulatory rate has been shown to be one of the prerequisites to the development of both bland and infective thrombi. It has long been appreciated that the rate of blood flow is retarded after operation and Dahl has recently reported actual roentgenological demonstration of delayed venous return from the lower extremities following abdominal surgery. Slowing of the rate of blood flow after operation is occasioned by the enforced bed rest and depletion of the general condition of the patient lowering of the blood pressure and weakening of the cardiac impulse. Venous stagnation is further favored by inhibition of the depth of respiration because of abdominal

pain, distention, and constrictive bandaging. The blood volume is reduced as a result of hemorrhage, restricted fluid intake and loss of body liquids through vomiting and diaphoresis.

Changes wrought in the composition of the blood by operation have been widely studied, and with varying results. Among those mentioned are increased viscosity, sedimentation rate, blood protein, fibrinogen, calcium, and platelets. Colloidal and electrical alterations, disturbances in the acid base equilibrium and qualitative changes in the platelets have all been reported. The clotting time and bleeding time have frequently been found to be shortened. Granted that such changes may accompany the postoperative or puerperal period, it is unlikely, as has been herein shown, that most of them could have any bearing on the thrombosis question. Hypothetical alterations in the agglutinative tendency of the platelets, which might, conceivably, predispose to their settling out and becoming agglutinated, do not lend themselves to demonstration.

Alterations in the vein wall might occur as a result of operative trauma to the vessel. It is difficult to see, however, how trauma during the ordinary laparotomy, particularly for lesions in the right upper quadrant, could sufficiently irritate the veins of the left lower extremity to produce thrombosis. Even phlebitides following appendicitis operations are predominantly left sided. Furthermore



Fig 3 Experimental thrombophlebitic edema. A Section of artery and vein following experimental thrombophlebitis, showing absence of marked periphlebitic inflammation.

the relatively long latent period between the operation and the onset of the vein complication speaks against operative trauma as an important factor in the etiology of thrombosis.

The rôle of infection is frequently adduced in the explanation of postoperative and puerperal phlebitides, and indeed, these complications are more common in patients in whom infection is present. However, this discussion of the avenues of infection to the veins emphasized the infrequency with which direct connection between the operative or placental site and the phlebitic vessel can be demonstrated. Infections probably increase the tendency to vein complications by adding to the impairment of the general condition.

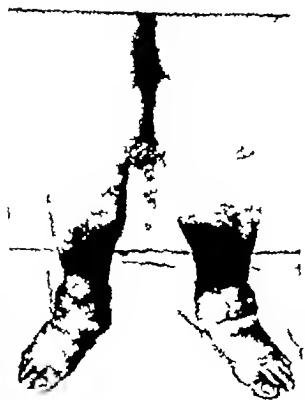


Fig 2 Phlebitic indurations from superficial vein phlebitis without marked varicosities, in patient who has had old, deep vein phlebitis.



Fig 4 Elephantiasis resulting from deep vein phlebitis.

prolonging the immobility and further retarding the rate of blood flow. Furthermore infection from the field of operation may provide the atrium from which bacteria are carried to the affected vein by the metastatic route. The rôle of infection may therefore be considered as indirect and contributory rather than determining.

**Relation to embolism.** Thrombosis and inflammation of the veins derive much of their significance from their ominous association with pulmonary embolism. The incidence, character and menace of the embolism depend upon the type of vessel which harbors the thrombus, and the intensity and nature of the coexistent phlebitis. A few general rules may be stated. The firmness with which the thrombus is attached to the vein wall is apparently in direct proportion to the degree of inflammatory reaction provoked. Most of the major emboli arise from static thrombi lying loosely in the vessel. Clinically recognizable thrombophlebitis antedates such embolism only in exceptional cases. Suppurative softening, however, results in the fragmentation of the thrombus with consequent showers of small infectious emboli which frequently lead to pulmonary suppuration or pyemia.

The size of the embolus naturally depends upon the length and lumen of the vein in which the antecedent thrombus is lodged. Massive emboli striking without warning and frequently bringing sudden and dramatic death must be large enough to obstruct one or more of the main branches of the pulmonary artery. Such a mass can come only from a major vessel, usually the iliac or femoral vein. Small emboli frequently result in pulmonary infarction, particularly if there is coexistent respiratory or cardiac impairment. Many of smaller size produce no detectable clinical disturbance. The infrequency of infection in infarcted lung has been offered as evidence of the non-bacterial origin of the thrombus.

#### PHLEBITIS AND THROMBOPHLEBITIS OF THE LOWER EXTREMITIES

Thrombosis and thrombophlebitis are especially likely to occur in the veins of the lower extremities. The clinical manifestations and the gravity of the disease depend in large

TABLE II.—CLASSIFICATION OF PHLEBITIDES OF LOWER EXTREMITIES

##### Phlebitis of varicose vein

- A Ascending type
- B Localized form

##### Phlebitis of non-varicose superficial vein

- 1 Acromioclavicular
- 2 Localized
- 3 Phlebitis migrans
- 4 Phlebitis of Bacter' disease

##### 3 Deep vein thromboses and inflammations

- A Suppurative thrombophlebitis of iliac vein
- B Non-suppurative thrombophlebitis—phlegmasia alba dolens
- C Blood thromboses

part upon the type of vein affected. Several years ago Homans suggested dividing the phlebitides of the lower extremities into three groups: those affecting the deep veins, those of normal superficial veins and those involving varicose veins. This convenient classification will be followed in this discussion (see Table II).

**Phlebitis of varicose veins.** Thrombosis and inflammation are extremely common in varicose veins, and most of the complications of varicose veins may be shown to be inflammatory in origin. In light of what has been said regarding the etiology of phlebitis it is not surprising that these veins which are subjected to stasis and its attendant pressure and anoxemia, provide a site of predilection for circulating organisms. Frequent degenerative changes in the lining endothelium further favor the development of thrombosis and inflammation. Conditions predisposing to thrombosis in general, such as operation, delivery, intercurrent infection, debility and trauma are frequently the immediate precursors of the phlebitis, although repeated attacks of spontaneous inflammation are extremely common in patients who consider themselves otherwise entirely well.

Homans called attention to the relative sickness of the clinical manifestations of varicose vein phlebitis as compared with that in normal vessels. He states further that the sequelæ of these inflammatory attacks are of little significance. This observation is not borne out by the study of large numbers of these patients. It can be shown rather convincingly that most of the complications of varicose veins, which are usually attributed to stasis and congestion are really inflammatory

in origin, and that there is a direct sequence of changes from the phlebitides to indurations, dermatoses, and ulcerations

The attack of phlebitis may follow a slight bruise or come in the train of an acute upper respiratory infection. Often no ascribable cause can be found. Two rather distinct varieties are seen. The inflamed segment may involve but 2 or 3 inches of the vein and remain localized to this area, or it may advance centrally and peripherally until most of the saphenous system is involved. Mild general symptoms may accompany the latter, in the former they are usually absent. The patient complains of slight pain in the involved area, and, on examination, a firm, dull red somewhat tender cord is seen. A variable amount of periphlebitis accompanies the attack. These inflammations pursue a subacute course, and recurrences in the same or other segments, are notoriously frequent.

In the progressing form of the disease, the inflammation almost invariably stops short at the saphenofemoral junction. Limitation of the process to the superficial veins has been convincingly explained on the basis of the difference in rate of blood flow in the superficial and deep venous systems. The circulation in the latter is sufficiently more rapid to prevent the extension of the phlebitis to the femoral vessels. The thrombus almost invariably canalizes so that the varicosity is rarely permanently obliterated by this process. Calcification of portions of the thrombus occasionally occurs, with formation of phleboliths which persist indefinitely. In rare cases, suppuration of portions of the thrombus may result in abscess which requires drainage.

The usual type of varicophlebitis remains localized, with greater tendency to recur at the same site. Eventually, the inflammatory changes extend from the vein wall to the adjacent skin and subcutaneous tissues. At this stage the lesion presents the appearance of a round or oval patch of low grade cellulitis. The skin is reddened and indurated, and there is slight pain and tenderness on pressure. The temperature may be elevated a fraction of a degree. These attacks, too, tend to recur, and as they recede, leave pigmentation and fibrosis. Ultimately, the skin over a limited

area, which sometimes involves a large portion of the circumference of the lower leg, becomes transformed into a dark brown, indurated zone with pigmentation, fibrosis, and atrophy of the overlying integument. These zones, which are spoken of as phlebitic patches or phlebitic indurations are the immediate precursors of varicose eczemas or of ulcers which show little tendency to heal.

That these changes are inflammatory, rather than merely stasic, can be convincingly demonstrated by following the lesion through its successive stages. The long axis of the patch is usually parallel with the course of the infected vessel, and in many instances, a varix may be palpated as a groove or channel passing through the board-like area. There is no parallel between the extensiveness of the varicosities and the severity of these skin lesions, nor does the area of involvement always lie in the most dependent portions where congestion would be most severe. Adjacent portions of the skin, separated from these indurations by only a few millimeters, retain their normal color and consistency. It is difficult to reconcile the sharp limitation of the process with chronic passive congestion, in view of the very rich overlapping of the cutaneous venous circulation. Finally, in support of the inflammatory genesis of these complications, it may be mentioned that conditions of known chronic passive congestion, such as occur in long standing cardiac decompensations, are not associated with indurations of the type described here, or their subsequent degenerations.

Aside from these local changes, which may become disabling, the prognosis in varicophlebitis is good. Embolism, the dreaded sequel to any phlebitis, is very rare. This is particularly true of the artificial, or chemical phlebitis induced by the therapeutic injection of varicose veins. Two factors of safety are mentioned in explanation of the infrequency of embolic accident following such injections, and these apply largely to the spontaneous phlebitides as well. The more important of these is the fact that the thrombus is inflammatory in its origin and is firmly adherent to the irritated and denuded vein intima. Such thrombi are not at all likely to become dis-

lodged as emboli. The second factor is the reversal of the direction of flow in varicose veins, as may be demonstrated by the Trendelenburg test. If portions of the clot did break loose while the patient was erect, they could not flow upward to enter the general circulation, but would of necessity go downward to be caught in the pre-capillary vessels, where they could do no harm. The rare emboli which do occur are of small size and give rise to minor pulmonary interctions. If infected suppuration might result.

**Treatment.** Inasmuch as the sequelae of varico-phlebitis frequently lead to distressing and even disabling end-results, their prevention constitutes the greatest indication for the early obliteration of varicose veins. Injection or ligation in the presence of active phlebitis, even of the subacute variety is dangerous, and such treatment should be postponed for several weeks or months after the inflammatory phenomena have disappeared.

Active treatment for this type of phlebitis is essentially conservative. Prolonged immobilization is unnecessary and most of these patients may be permitted to be ambulant throughout. If the involved vein segment is below the knee the limb should be encased in an Unna's paste boot, which is renewed periodically. This relieves the edema and congestion, and materially alleviates the discomfort. When the inflammation has subsided further support by means of woven elastic bandages, for an additional period of several months is advisable. The progressing type of phlebitis involving the saphenous trunk in the thigh is not amenable to this simple therapy and rest, elevation and the application of hot compresses may be required. The progress of the lesion may sometimes be checked by compressing the trunk of the vein above the highest point of involvement by means of a felt pad held in place with a strip of adhesive tape. Obliteration of the trunk in advance of the lesion by injection or ligation has been advised by some writers, and, in my opinion, may be indicated in cases in which showers of small emboli are being thrown off. This latter eventuality rarely occurs. After an adequate period of quiescence cautious treatment for the underlying varicosities

should be instituted. If the first small, tentative injections produce no excessive inflammatory response active obliteration by means of injection, together with ligation if necessary should be carried out.

**Phlebitis of non-varicose superficial veins.** Superficial veins of the lower extremities which are not varicose are also subject to phlebitic inflammation. Such normal vessels are much less frequently involved, however than are those previously dilated and varicose. The difference in incidence may readily be explained by the relative absence of stasis and of degenerative intimal changes in the intact veins. The clinical course and the sequelae of phlebitis of these veins closely resemble those of inflamed varicosities. Homans stresses the benignity of phlebitides of varicose veins as compared with normal superficial vein inflammations, and explains the difference on the basis of gradual adaptation of the lymphatics during the period of stretching and dilatation of the veins, so that when the eventual phlebitic lymphangitis occurs, no crippling of the lymphatic return takes place. Our experimental observations, which will be discussed later and my clinical experience is at variance with this view. Edema of the extremity is not part of the picture of superficial vein pathology whether those superficial veins be normal or varicose and the local cutaneous changes are equally severe in both types of phlebitis. As was stated before, they rest upon direct inflammatory changes emanating from the inflamed vein segment, and are not directly due to stasis in either the venous or lymphatic channels.

Phlebitis of normal superficial veins may be spontaneous or may result from local infections in the vicinity of the affected vessel. I have seen progressive thrombophlebitis of the entire saphenous vein following a localized third-degree burn on the dorsum of the foot. These inflammations are also prone to occur after operation, childbirth, or trauma, and may complicate infectious diseases or cachectic states. They are particularly common in limbs which have been the seat of deep vein phlebitis, many of the distressing and disabling sequelae of which may be due to associated or secondary superficial vein infection.

The clinical manifestations of this type of phlebitis are similar, as stated, to those described of the varicose vessels, although they may be somewhat more acute. The same two rather distinct varieties are seen. The progressive or advancing type commonly occurs after operation or delivery. It usually involves the trunk of the long saphenous vein and frequently begins in the upper portion of the thigh. It is ushered in with fever and pain in the limb, and a firm, tender, reddened cord may be detected along the course of the saphenous vein. General edema of the leg does not develop. The process may progress downward to involve the entire saphenous system and occasionally may extend to the communicating veins which anastomose the superficial with the deep systems. When the process subsides, the thrombus canalizes and the lumen of the vein is restored. The wall is somewhat thickened and the valves within the diseased segment, as a rule, are completely destroyed. Homans has pointed out that although the circumference of these vessels may not be materially increased, the absence of functioning valves permits a much greater degree of regurgitation than occurs in extensively dilated and tortuous varicose veins. In the exceptional case in which the valves in the communicating as well as the saphenous veins are crippled, reflux takes place through both channels, with very serious derangement of the venous return from the skin areas of the leg.

The localized form of superficial vein phlebitis usually occurs in the calf or lower half of the leg, frequently spontaneously or after slight trauma. It is more common in women, usually in those of middle age, and resembles in its clinical manifestations and sequelæ, the ordinary form of localized phlebitis of varicose veins. Many so called varicose ulcers arising in the absence of demonstrable varicose veins are due to this type of phlebitis. It has a special predilection for limbs which have harbored deep vein infections, and leads to indurations, dermatoses, and intractable ulcerations, all of which materially aggravate the distress and disability of this unfortunate group of patients.

Major embolism does not complicate superficial vein phlebitis. Repeated small infarcts

may result from dislodged fragments of thrombus from the advancing type of phlebitis, they are rare in the localized form. Treatment of both forms is similar to treatment of the corresponding types in varicose veins. Rest, elevation, and heat usually suffice for the progressive form. Showers of emboli may require ligation. When the process has entirely subsided, the resulting incompetent vein may require obliteration preceded, perhaps, by ligation. Supportive treatment with the Unna boot materially alleviates the inflammation, and also relieves the pain and itching and promotes the healing of the resulting eczemas and ulcers. These phlebitides are notoriously prone to recur, each succeeding attack increasing the induration and discoloration, and adding to the permanent, irreversible impairment of the tissues. Constant supervision is therefore necessary, with prompt treatment at the first sign of recurring trouble. In the intervals between attacks, measures directed toward improving the circulation, including contrast baths and diathermy may be indicated.

*Phlebitis migrans and the phlebitis of thromboangitis obliterans.* A form of superficial vein thrombophlebitis has been singled out as an entity under the name of phlebitis migrans. This rather uncommon disease affects males predominantly, usually those of youthful or middle age. It is characterized by recurring attacks of low grade inflammation of the superficial veins, usually involving localized segments of the saphenous trunk or its tributaries, and frequently displaying a roughly symmetrical distribution. Its course is marked typically, by periodic subsidence and recurrence in the same or other segments of superficial veins. Extension to the deep vessels, and involvement of visceral veins in the chest and abdomen have been reported. There are no specific pathological or bacteriological findings.

Lesions of this type have been described by Paget, as manifestations of gout. Similar affections have been attributed to syphilis or have been observed as complications of rheumatic fever and other diseases. Buerger has called attention to the frequent occurrence of patches of superficial vein phlebitis, resembling those here described, in patients with



thrombo-angitis obliterans. This finding has been widely confirmed, and recurring superficial phlebitis is now considered highly suggestive of Buerger's disease. This raises the suspicion that many of the so called "idiopathic" and gouty forms of phlebitis migrans may actually have been early manifestations of thrombo-angitis obliterans. Cases have, in fact, been reported by D Abreu and others in which Buerger's disease was recognized as long as 40 years after the onset of the migrating thromboses. Since recurrence is a characteristic feature of superficial vein phlebitis in general and in view of the absence of pathognomonic morphological and bacteriological findings, and inasmuch as many of these lesions are part of the picture of Buerger's disease the justifiability of considering phlebitis migrans a clinical entity may be questioned.

#### PHLEBITIS AND THROMBOSIS OF THE DEEP VEINS

By far the most important group of vein occlusions and inflammations, from the standpoint of severity of their clinical manifestations, sequelae, and danger to life, are those involving the deep veins. These vary in degree of inflammatory reaction from the suppurative thrombophlebitides secondary to purulent postpartum or postabortive pelvic infections, through the ordinary deep vein phlebitides as they occur after operation or delivery—the so called phlegmasia alba dolens—to the bland thromboses of the iliac and femoral veins whose existence is unsuspected until a massive and perhaps fatal pulmonary embolism supervenes. Some degree of inflammatory reaction as has been emphasized before is always present, whether it be the primary factor or secondary phenomenon, or merely the reparative reaction to a simple static thrombosis.

Suppurative phlebitides extending into the iliac vessels from purulent infections in the pelvis, by way of the uterine veins, are characterized essentially by septic phenomena which may lead to multiple abscesses in the pelvis, or to fatal septicemia or pyemia before local signs of vein occlusion appear. Repeated chills, high remittent fever, intense toxemia, and delirium dominate the picture. Circulatory

disturbances in the lower extremity such as cyanosis or edema, are not observed. Massive embolism is infrequent. Showers of small septic emboli often give rise to septic infarcts or pneumonias or even to generalized metastatic pyemic abscesses. The prognosis in this type of phlebitis is always grave, and heroic therapeutic measures, such as the intra-abdominal ligation of the iliac veins or the intravenous injection of antiseptic dye solutions may reasonably be considered.

The usual non-suppurative postoperative or postpartum thrombophlebitis, long recognized under the name of milk leg or phlegmasia alba dolens, presents a characteristic picture. The lesion may develop at any age, and is more frequently seen after septic operations or deliveries. The onset of the vein infection is frequently announced by a chill, which may be repeated, and a rapid rise in temperature. The patient complains of pain in the leg or thigh, stiffness, and loss of motion. The limb begins to swell, the edema usually appearing first in the lowermost portions of the leg. Its upward extent depends upon the degree of venous occlusion. The leg becomes uniformly swollen, tense, white and shiny and pits on pressure. There may be tenderness along the course of the deep vessels. Fever persists for days or weeks and after subsidence, may recur. The edema disappears in the milder cases, to recur for a short time when the patient begins to be up and may then vanish entirely. In more severe involvements, the edema persists for a number of months and in some cases is permanent. These familiar porky edemas may be a source of severe discomfort and disability especially if repeated attacks of an erysipelas-like streptococcal cellulitis supervene. The skin then becomes thickened and infiltrated and a true elephantiasis may develop. Late superficial vein inflammations, with their sequelae of indurations, dermatoses, and ulcers are frequently superimposed upon the picture, as was mentioned before, thereby adding materially to the distress and disability of these unfortunate sufferers.

The cause of the edema which follows thrombophlebitis has long been disputed. Two principal explanations have been offered,

one ascribing the edema to interference with the venous return, the other attributing it to inclusion of the main lymphatic channels in the perivenous inflammatory reaction, resulting in lymph stasis which is considered the source of the edema. We have shown (31, 32, 33, 34) that mechanical interruption of the lymphatics of the limb of the experimental animal does not result in edema. Extensive peripheral obstruction of the main veins, however, by means of even the blandest thrombi, uniformly results in massive edematous swelling of the extremity. India ink emulsion injected into the feet of animals at the height of experimental edema can be recovered from the iliac lymph nodes, indicating patency of the lymphatics. This, together with the absence of microscopic evidences of perivenous inflammation in these experiments, would make it seem that the lymphatic theory of postphlebotic edema is not tenable, and that the swelling is to be explained on the basis of insufficient venous return.

A second factor which may add to the swelling of the leg is the collateral inflammatory edema which accompanies the infected portions of the vein. Some authors limit the usage of the term "phlegmasia alba dolens" to those cases in which the edema is inflammatory rather than circulatory in origin. The former is supposed to begin in the upper portions of the thigh, and extend downward with the advance of the phlebitis. The latter is said to appear first in the most dependent portions, its upward extent depending upon the degree of circulatory embarrassment. It seems to me the distinction is difficult and unnecessary, nor was it made when the term was first applied (29). These cases are better considered as a single group, and the term "milk leg" or "phlegmasia alba dolens," if used at all, should cover all cases of postoperative or postpartum thrombophlebitis with edema.

Thrombophlebitis of this type is often feared as the source of fatal pulmonary emboli. While embolism does occur, it is relatively infrequent, and more often than otherwise, takes the form of pulmonary infarction which causes little or no clinical disturbance, or which may simulate pneumonia. The relative

infrequency of embolic accident is explained by the material degree of inflammation which accompanies and fixes the thrombus. Furthermore, the veins in these cases are completely occluded, as is evidenced by the dependent edema. A thrombus in such a vessel is much less likely to break loose than is one lying within a vein through which the blood is still flowing.

The status of the venous return from the extremity after recovery from a deep vein thrombophlebitis has received but little attention in the literature. In some cases, the edema disappears entirely. In many others, its persistence for indefinite periods indicates, among other things, that the venous drainage has been permanently damaged. Actual, persisting occlusion of the principal deep veins is extremely uncommon, in spite of the usual textbook warnings to rule out deep vein closures before destroying superficial veins. In an extensive material, over a number of years, I have seen but two instances in which I was convinced that the deep veins remained impatent. In the vast majority of patients who have had deep vein thrombophlebitis, evidences may be found to show that the lumen of the veins has been restored. If superficial varicosities are present, the Trendelenburg and Perthes tests almost invariably point to patency of the deep veins. The edema usually subsides, at least in part, with recumbency or elevation of the extremity, and recurs when the patient is up and about. These findings indicate that canalization of the thrombus almost always follows deep vein inflammations. The restoration of the lumen, however, is accompanied by a destruction of the valves, resulting in a relative functional insufficiency of the venous return.

In our studies of thrombophlebotic edema, the protein content of the edema fluid was found to be relatively high, values between 3 and 4 per cent often being recorded. Of the multiplicity of factors involved in maintaining the water balance between the capillaries and the tissue spaces, the colloid osmotic tension exerted by the plasma proteins of the blood is recognized as one of the important elements in the return of fluid from the tissue spaces to the blood vessels. The extravasation of

edema fluid containing a high concentration of these same proteins tends to equalize this colloid osmotic tension and interferes with the fluid return. In later stages, there are probably irreversible changes in the tissues, of a physical nature which further tend toward perpetuating the edema. It would, therefore, seem therapeutically important to hasten as much as possible, the resorption of the edema in the acute stage. We have demonstrated in our experimental studies, that the disappearance of this type of edema may be accelerated by the intravenous use of mercurial diuretics such as salyrgan by the parenteral administration of calcium salts and parathyroid hormone and by X-ray therapy. These features have been included in our management of acute thrombophlebitides with edema.

Treatment during the acute stages of iliac and femoral thrombophlebitis is directed toward the prevention of embolic accident, the acceleration of the resorption of the accompanying leg edema, and symptomatic relief for the associated discomfort. The former requires rigid bed rest, elevation, and the avoidance of all massage, manipulation and rough handling which might dislodge a portion of the thrombus. These precautions are observed in spite of the fact that massive embolism is an uncommon complication in this group of vein lesions. The duration of the enforced rest is still a perplexing question. Varying periods ranging from 10 days to 6 weeks after the temperature has become normal have been arbitrarily established by various writers. The tendency of late has been to shorten this time. In a recent publication, do Takats has described a management of cases of this type in which gradual exercise and massage are begun after 10 days of normal temperature which allows the patient out of bed during the fourth week.

Early mobilization of the edema is effected by elevation, restriction of the salt and fluid intake and administration of salyrgan intravenously in doses of 1 to 2 cubic centimeters. Ammonium chloride may also be given. Halban has advocated X-ray therapy during the acute stages of the disease. Our experiments revealed that X-ray irradiation accelerated the rate of fluid absorption in postphlebitic

edema. In a few cases treated with X-ray rapid subsidence was noted. Calcium and parathyroid therapy has long been empirically employed to hasten absorption of exudates. Experimentally too, this regimen was found to hasten the disappearance of the edematous swelling. As soon as the subsidence of the inflammation permits, graded exercise, cautious massage, and diathermic treatments are instituted. Support by means of elastic bandage or stocking is advised for a period of 3 to 6 months and longer if the edema persists.

In the chronic stages of phlebitic edema, particularly in those associated with indurations, ulcerations or elephantiasis changes, treatment is difficult and unsatisfactory. The Unna's paste boot offers an almost ideal means of obtaining elastic support, whereby the edema may be reduced, the indurations softened and the ulcers healed. When maximal improvement has been attained, further supportive treatment with elastic bandages or stockings is advised and massage and diathermy are employed. Constant supervision is necessary in order that recurrent inflammations may be recognized and controlled before extensive ulcers again develop.

Surgical procedures such as the Koonoleon operation, which are directed toward the establishment of additional communications between the superficial and deep lymphatics of the leg are frequently advised for the elephantiasis which may complicate post phlebitic states. As was shown by our experimental investigations, the hypothesis upon which these operations are based is untenable because the lesion is one of the veins rather than of the lymphatics. Furthermore the primary site of inflammation is generally considered to be in the iliac and femoral vessels. Both superficial and deep lymphatics drain into the trunks surrounding these veins. It is difficult to see how anastomosing the lymphatics even if it were possible distal to the site of obstruction could affect the lymph drainage of the extremity. Nevertheless, experience in our own and other clinics attests the value of the Koonoleon procedure in cases of this type. The improvement resulting can probably be explained on the basis of the excision of irreversibly altered skin and sub-

cutaneous tissue, rather than upon the improvement of the lymphatic circulation

*The bland thromboses* of the main veins of the lower extremities differ sufficiently in their clinical manifestations from those already described to warrant separate consideration. This is especially true because of their sinister relation to pulmonary embolism. From many sources there have been statistical reports showing an appalling increase in the frequency of thrombosis and embolism. This is particularly true of the German literature, and, to a lesser extent, of the French and British reports, and applies to medical as well as post-operative material. According to Rosenthal, a similar increase has not been observed in the United States. Many factors have been blamed for the increase in thrombosis, including the impaired post-war nutritional states, the increase in intravenous medication, and the broadening of surgical indications to include many patients of advanced age, in late stages of disease, and with impaired hearts and blood vessels, who offer greater predisposition to vein complications. Because of the importance of thrombosis and embolism as a cause of postoperative death, the study of all possible predisposing influences and their eradication is of the greatest importance.

As a result of their insidious onset and the absence of striking clinical signs to indicate their existence, a sudden fatal embolic accident during convalescence from an otherwise uncomplicated operation is usually the first intimation that a thrombosis has occurred. Examination of the case records in retrospect often reveals a subfebrile elevation of the temperature for several days before the embolism occurred, which might have given an intimation that a thrombus had formed. A step-like rise in pulse rate has also been described as a diagnostic sign which, however, has been found lacking as often as it was present. Ducuing and his collaborators have closely studied the symptoms of simple thrombosis, and have described in detail various types of pain, spontaneous and induced by pressure or exertion, which may permit the early diagnosis of thrombosis and appropriate prophylactic immobilization. They list three sites of predilection for this

pain in the foot, the calf, and the thigh, and believe that careful search and attention to these symptoms have permitted diagnosis of thrombosis in a far larger percentage of cases than is usual, and that the resulting immobilization has materially reduced the incidence of embolic accident.

The prognosis in bland thrombosis is always grave because of the ominous tendency of these static, non-adherent clots to become detached as emboli. Furthermore, the lesion characteristically involves the large veins of the pelvis and lower extremity, so that emboli which do break loose are often sufficiently large to occlude the main branches of the pulmonary artery and lead to immediate or early death of the patient.

Treatment for thromboses must necessarily be largely prophylactic, since the presence of the condition is usually unsuspected. The factors responsible for thrombosis have been enumerated. The most important of these, slowing of the circulation, is the one most readily avoided. Efforts to combat the lowered blood pressure and slowed circulation have consisted in the avoidance of constricting bandages, the inhalation of carbon dioxide to promote deeper respiration, the administration of thyroid extract, the use of systematic exercises beginning immediately after operation, and the early mobilization of surgical patients. Experience in getting patients out of bed within the first 2 or 3 days after laparotomy has accumulated in various clinics over a period of years. It has been found to be safe, beneficial to the general physical and mental well-being of the patient, and effective in reducing the incidence of thrombosis and embolism. In patients too debilitated to permit mobilization, systematic bed exercises afford the best substitute. These should find introduction in the postoperative management of all patients after major surgical procedures.

Active treatment for thrombosis presupposes its diagnosis before embolism has occurred. If it is at all suspected because of subfebrile temperature elevation, tachycardia or pain in the foot or leg, the greatest possible caution to prevent dislodging emboli would be called for. This would entail the gentlest

possible handling during nursing care, particularly during the bath and in the use of the bed pan. Because the presence of the thrombosis can only be suspected, the efficacy of any management cannot be clearly evaluated.

A few patients have been rescued from embolic death by successfully executed Trendelenburg embolectomy. Credit is due the surgeons who have saved lives by this heroic measure. The difficulty of being on hand when the accident occurs, the uncertainty of diagnosis, the severity of the intervention, and the haunting question as to whether the patient might not have survived if not operated upon will probably keep the Trendelenburg operation a rare occurrence, and the patients saved by it exceptional indeed. In prophylaxis rather than in therapy is our hope.

#### SUMMARY

1. Phlebitis, thrombosis, and thrombophlebitis are considered under a single heading because the three terms are frequently interchanged, and because there is no clear-cut differentiation between them. Phlebitis is usually accompanied by thrombosis and even the blandest thrombosis provokes an inflammatory reaction of the vein wall. It is often impossible to determine whether it is the thrombosis or the phlebitis which is the primary condition.

2. Thrombosis consists of the agglutination of platelets along the vessel wall to form a homogeneous mass. Superimposed upon this is a deposition of white blood corpuscles. Fibrin formation plays no part in the origin of the thrombus but may occur at its periphery as a result of the liberation of ferments from the agglutinated platelets and corpuscles, which results in the coagulation of the adjacent blood mass.

3. Thrombosis is due to the interaction of two or more of the following causes: Slowing of the circulation, which is probably the most important factor; changes in the vessel wall, which is the initiating factor in some types, but of secondary importance in others; and alterations in the composition of the blood. The latter are probably more important in the propagation of a thrombus already formed than in its origin.

4. Phlebitis may be merely the reparative reaction to a bland thrombosis, may be due to metastatic infection, may reach the vein by extension from a suppurative process about the radicles of the vessel, or may result from direct injury or infection. Veins have a remarkable capacity for harboring latent infections, and periodic activation frequently occurs.

5. Vein complications frequently follow delivery or operation. The changes induced in the organism by these procedures consist of slowing of the circulation and, perhaps, as yet undemonstrable blood changes. Infection indirectly favors the development of vein disease by providing an atrium for infecting organisms and by further slowing the circulatory rate.

6. The danger of embolism is inversely proportional to the amount of inflammation accompanying a thrombus. Suppurative softening may lead to showers of small infective emboli. Massive and perhaps fatal emboli can arise only from major vessels, usually iliac or femoral veins. Smaller emboli may produce little or no clinical manifestations.

7. Phlebitis is the most common complication of varicose veins, and a direct sequence of inflammatory changes leads from the phlebitis to ulcers and eczemas. Two forms are described. The clinical manifestations are mild. Treatment consists in supportive therapy followed by obliteration of the veins when the phlebitis has subsided.

8. Phlebitis of non-varicose superficial veins occurs much less frequently than varicose vein phlebitis. The two conditions resemble one another closely in their types, clinical manifestations and sequelae. Non-varicose vein phlebitis is particularly frequent in patients who have had deep vein infections, and materially aggravates the distress and incapacity thereby produced.

9. Deep vein phlebitides are divided into three forms: suppurative thrombophlebitis secondary to purulent pelvic infections is frequently rapidly fatal; non-suppurative thrombophlebitis phlegmasia alba dolens, produces a characteristic picture: edema, transitory or permanent, forms an essential feature of this picture. Bland thrombosis is

usually not recognized until a massive pulmonary embolism has occurred. Treatment is therefore of little avail, and prophylaxis is of predominant importance

# BIBLIOGRAPHY

- 1 ASCHOFF, L Thrombosis Arch Int. Med, 1913, 12 503
- 2 Idem Thrombosis Lectures on Pathology New York, 1924
- 3 ASCHOFF, L, BECK, B, DE LA CAMP, O, and KROENIG, B Beitrage zur Thrombosenfrage. Leipzig, 1912
- 4 BAUMGARTEN, PAUL v Entzuendung, Thrombose, Embolie und Metastase Munich, 1925
- 5 BIZZOZERO Quoted by Eberth and Schimmelbusch.
- 6 BUERGER, L The veins in thromboangitis obliterans J Am. M. Ass., 1909, 52 1319
- 7 Idem. The Circulatory Diseases of the Extremities Philadelphia, 1924.
- 8 D'ABREU, A L Relation of thrombophlebitis migrans to thromboangitis obliterans Brit. M. J., 1934, 1, 101
- 9 DAML, J Postoperative Roentgenuntersuchungen. Zentralbl. f. Chir., 1933, 60 1162
- 10 DE TAKATS, G "Resting infection" in varicose veins, its diagnosis and treatment Am. J. M. Sc., 1932, 184 57
- 11 Idem The management of acute thrombophlebitic edema J Am. M. Ass., 1933, 100 34
- 12 DUCUING and collaborators
- a. DUCUING, J Quelques notions étiologiques sur les phlébites chirurgicales et obstétricales J méd franç., 1934, 23 43
- b. DUCUING, J, and THOMAS. La douleur dans les phlébites chirurgicales et obstétricales du membres inférieurs et du bassin. J méd franç., 1934, 23 50
- c. DUCUING, J, and FANRE, P C. Héus post-opératoire et phlébite pelvi abdominale. J méd franç., 1934, 23 55
- d. DUCUING, J Rapports entre les phlébites chirurgicales et obstétricales du pelvis et celles des membres inférieurs J méd franç., 1934, 23 63
- e. GUILLIEM, P Le dépiçage précoce de la phlébite puerpérale J m d franç., 1934, 23 69
- f. JEANTY, J Les anticoagulants chimiques dans la prophylaxie et le traitement des phlébites chirurgicales et obstétricales J méd franç., 1934, 23 72
- g. DUCUING, J, and GUILLIEM, P Lever précoce et "promenade au lit" dans le traitement des phlébites chirurgicales et obstétricales J méd franç., 1934, 23 74
- 13 EBERTH, J C., and SCHIMMELBUSCH, C. Die Blutplättchen und die Blutgerinnung Arch f path Anat., 1885, 101 201
- 14 Idem. Experimentelle Untersuchungen ueber Thrombose. Arch f path Anat., 1886, 103 39, 105 331
- 15 HALBAN, J Strahlenbehandlung bei Thrombophlebitis Wien klin. Wchnschr., 1930, 43 1368
- 16 HAYEM. Quoted by Eberth and Schimmelbusch.
- 17 HOMANS, J Thrombophlebitis of the lower extremities Ann Surg., 1928, 87 641
- 18 Idem. Phlegmasia alba dolens and the relation of the lymphatics to thrombophlebitis Am. Heart J., 1932, 7 415
- 19 HUNTER, JOHN A Treatise on Blood, Inflammation, and Gunshot Wounds. Philadelphia, 1817
- 20 KENDALL, A. I., and JACQUES, L Personal communication.
- 21 KISTLER, H. D Thrombophlebitis of the left leg J Am. M. Ass., 1912 59 437
- 22 KRISTENSON, A. Zur Kenntnis der lokalisierten Thrombenbildung in der Vena iliaca communis sinistra Acta med Scand., 1930, Suppl 33
- 23 MACMURRICH. Quoted by Kristenson
- 24 PAGET, J Quoted by Welch.
- 25 ROSENTHAL, S R. Thrombosis and embolism. J Lab & Clin Med., 1930, 16 107
- 26 Idem. Thrombosis and fatal pulmonary embolism Arch Path., 1932, 14 215
- 27 VIRCHOW, R. Thrombose und Embolie. Leipzig 1910
- 28 WELCH, W H. Thrombosis Albutt and Rolleston's System of Medicine. Vol 6 London 1909
- 29 WHITE, C An Inquiry into the Nature and Cause of that Swelling in One or Both of the Lower Extremities Which Sometimes Happens to Lying in Women. London, 1784.
- 30 ZANN Quoted by Baumgarten.
- 31 ZIMMERMAN, L M Complications and treatment of varicose veins Illinois M. J., 1931, 51 60
- 32 ZIMMERMAN, L M., and DE TAKATS G The mechanism of thrombophlebitic edema Arch Surg., 1931, 23 937
- 33 ZIMMERMAN, L M., and LIEBERMAN, A. L The therapeutic effects of calcium gluconate on thrombophlebitic edema J Pharmacol & Exper Therapy, 1933, 48 301
- 34 ZIMMERMAN, L M GALLT, J T HALPERN, S S and DE TAKATS, G The effects of salyrgan and X ray on the rate of disappearance of thrombophlebitic edema J Lab & Clin Med., 1933, 19 243
- 35 ZURHILLE, E. Thrombose und Embolie nach gynae kologischen Operationen. Arch f Gynaec 1908, 84 44
- 36 Idem Experimentelle Untersuchungen ueber die Beziehungen der Infektion und der Fibringerinnung zur Thrombenbildung in stromenden Blut. Beitr z path Anat. u allg Path., 1910 47 539

# CONSERVATIVE AND RADICAL MEASURES IN THE TREATMENT OF ULCER OF THE LEG<sup>1</sup>

A STUDY OF TECHNIQUES, INDICATIONS, AND RESULTS

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THE increased incidence of chronic leg ulcer in this and in other countries caused by modern living conditions has lately stimulated widespread interest. The difficulty of accomplishing cure has been a great challenge of recent years for a more adequate study of the problem. The manner in which this challenge has been met and in which treatment has been put on a more rational basis will be described in this report and a second one which will follow.

Until lately treatment has been needlessly complicated and expensive while results have generally been unsatisfactory. Referring to England, A. Dickson Wright says

"One realizes what terrible cause varicose ulcer is to the lower classes of this country. It is much more prevalent than is imagined, because most of the sufferers, tired of receiving no relief from the medical profession, write down to endure their complaint with occasional extravagance in the form of quick remedies. In every large town of the mad lands may be found an institution, under the supervision of unqualified people, for the treatment of 'bad legs'."

It is equally true that varicose ulcer is very prevalent in this country. A patient with an ulcer of the leg is at a great disadvantage but the unfortunate individual with a large indolent one as a rule leads a very unhappy life and invariably is almost a total economic loss. One apparently healthy man of 40 who recently came to the Vanderbilt University Dispensary had been out of work for a year and a half because of two extensive leg ulcers which, with the usual medical attention and home care had refused to heal. As far as his incapacity was concerned he might as well have been suffering from advanced pulmonary tuberculosis. The problem was made more difficult by the man's desire to work when he was really unable to do so. Such patients as this one are seen in private practice rather infrequently but in our experience they are extremely abundant in the surgical dispens-

aries of this country. At Vanderbilt University Hospital in the past four and a half years 334 patients presented themselves for treatment of chronic leg ulcer. During 1933, 83 such patients were treated—an increase of 35 over the previous year.

Only within the last few years have any reliable techniques been worked out for the cure of leg ulcer. These developments have come about along two different lines of approach—the one employing radical or operative measures the other conservative or non-operative. Both require as a preliminary procedure the treatment of any underlying or predisposing cause of ulceration such as varicose veins or syphilis.

Radical treatment by excision and skin grafting will yield excellent results in the vast majority of cases. Recently we have described our technique employing a full thickness graft of a modified type—the perforated or sleeve graft, and have reported a series of cases (2, 3) cured by this procedure.

With the establishment of precise and clear cut indications for the use of these two techniques—the radical and the conservative—we have found that almost all non-malignant ulcers of the leg may be cured. Since we have already described the radical or operative technique elsewhere we will proceed with a description of developments in conservative methods and will finally state our conclusions as to the indications for each.

## CONSERVATIVE TREATMENT

The chief contribution of recent years in conservative measures has been the development of the elastic adhesive plaster technique. This development has undoubtedly been a gradual evolution brought about by efforts toward simplification in the treatment of leg ulcers. It appears to be an effective combination of four methods, each of which has been previously employed in the treatment of this

condition. It combines in one bandage the protective and supportive qualities of an Unna's paste boot, the elastic qualities of a rubber stocking, the porous qualities of a gauze dressing, the non-slipping fixative qualities of adhesive.

#### MATERIAL

The elastic adhesive bandage in its usual form consists of a thin adhesive plaster mass coated on a cloth bandage. The cloth is known as domette and is so woven as to be quite elastic. It may be stretched lengthwise to about one fourth again its length and regain its original size when it is released. The width remains practically unaltered when the bandage is stretched. The adhesive mass is also elastic. While the exact proportions of its ingredients have not been made public, according to one manufacturer it contains para-rubber, rosin, organic fat, amylum, and approximately 30 per cent zinc oxide. Another states "There is being used pure zinc oxide in conjunction with pure para-rubber and some medication," and adds that the plaster mass is produced in such a way that its elasticity is equal to that of the elasticity of the bandage. The loose weave of the cloth and the fact that the adhesive coating is thin, allow the bandage to be sufficiently porous to permit fairly free discharge to occur from an ulcer. Since the bandage is practically waterproof exudate may be washed from its external surface without disturbing it. We have used two preparations with good results. These are an imported German plaster "Iomoplast,"<sup>1</sup> and a second called "elastoplast,"<sup>2</sup> manufactured in this country. A third is also on the market, viz an English preparation prepared by the formula of A. Dickson Wright and known as "flexoplast."<sup>3</sup>

Most of our studies have been made while using the "Iomoplast" but recently this has been difficult to obtain and we have substituted the "elastoplast." The "Iomoplast" seems to require greater force to stretch it than the "elastoplast," and this seems to us to be an advantage although we have no absolute proof of this point.

We believe that Wright is responsible for first pointing out the advantages of a bandage of this type in promoting the healing of varicose leg ulcers. In May, 1930 (5) and again in December, 1930, Wright (6) emphasizes the unusual results which he had obtained with this dressing. The next year (7) he published a report with a grand total of "525 cases of cured ulcer of a total area of a little over twenty-five square feet." The largest of these, 180 square inches (or  $1\frac{1}{4}$  square feet), healed as readily as any. In this series there were relapses in only 3.4 per cent in 3 years, and all yielded easily to treatment. These results are especially striking when one considers how many patients with varicose ulcer ordinarily drift from place to place.

#### FIELD OF USEFULNESS

Granted that varicose leg ulcers form the commonest class of cases amenable to treatment by elastic adhesive they are still only one of many classes of cases in which it is useful. I have used it very successfully in promoting healing in many other types of leg ulcer such as traumatic, syphilitic, and trophic, as well as in ulcers from burns, and decubitus, and open wounds resulting from the operative removal of skin for grafting (Figs 1 and 2). In short it forms an excellent protective and semi-occlusive strapping for any superficial wound which is not acutely infected and in which there is so much loss of skin that suturing is impracticable.

Since elastic pressure is needed for varicose veins it is especially useful as a spiral bandage in covering both veins and ulcers in the lower extremities but I have also used it as a simple covering for ulcers on the upper extremities and for wounds on other parts of the body. Its use in clean wounds from burns and in skin grafted areas will be described in a separate article now in preparation.

#### TECHNIQUE OF TREATMENT

*Treatment of underlying causes of ulceration.* In every case the cause underlying the ulcer formation should be determined if possible and remedied either before or during the local treatment with elastic adhesive. General measures should always include a thorough

<sup>1</sup> May be obtained from G. Kuhlmann, 62 W. 45th Street, New York City.

<sup>2</sup> May be obtained from The Duke Laboratories, Inc., Long Island City, New York.



physical and laboratory examination. Many patients with ulcers suffer from secondary anemia. This should be remedied and a properly balanced diet including the necessary vitamins should be prescribed. The general condition of these patients is a very important factor in their healing. Syphilis is a not infrequent cause of leg ulcer. When present, treatment will aid materially in the rapidity of healing. Granuloma inguinale and tuberculous ulcers of the skin will each need appropriate general measures until the specific infectious agent is eradicated. In chronic osteomyelitis dead bone must be removed and the cavity must be allowed to fill up by granulation before the remaining ulcer is strapped. Peritonitis is usually secondary to ulceration, and will not require any especial treatment. If however bony spurs form as may frequently happen in the region of the foot or ankle, these should be excised. It goes without saying that in decubitus the local cause should be removed before treatment of the ulcer. When elephantiasis exists its treatment, if operative, should precede that of the ulcer. A very persistent multiple ulceration of the legs due to infection by *Staphylococcus aureus* is rather common in children. Autogenous vaccine during treatment has proved of value in about half of these cases. Lastly to this admittedly incomplete list, we add varicose veins. Very few ulcers will heal without recurrence unless varicose veins are remedied. Many will heal quickly when this is done. Newell and others have pointed out the superiority of the sclerosing treatment to operation in the vast majority of cases. It is the only means of satisfactorily treating veins in ambulatory cases. We believe nevertheless, that some veins high up in the thigh should be stripped and the saphenous ligated in order to avoid recurrence both of the veins and of the ulcers.

This list of predisposing causes while not complete may serve to emphasize the necessity of a careful diagnosis and treatment of underlying causes of ulceration before making an attack upon the ulcer.

*Preliminary local treatment of ulcer.* In case the ulcer area is suppurating only moderately this step may be omitted. In fact some

authors advise beginning the elastic strapping immediately no matter how soiled the area. In cases in which there is marked suppuration it is our custom over the ulcer and surrounding skin to use packs of gauze covered with cellophane or oiled silk and soaked with a saturated solution of boric acid. The latter may be introduced under the edge of or through a small opening in, the cellophane, and renewed at 4 hour intervals. A warm water bag is used for heat over the dressing. These packs are changed at intervals of 24 to 48 hours and are kept on until the granulations are healthy in appearance and suppurating only slightly. The ulcer is then considered ready for the third step in the treatment.

*The technique of applying elastic adhesive strapping.* The application of the elastic adhesive plaster to a wound seems very simple. It is nevertheless necessary to adhere strictly to certain details if the best results are to be obtained: (1) shave any hair bearing skin in the region to be covered. (2) If preliminary treatment (second step) has not been carried out cleanse the skin with alcohol and both the skin and ulcer with ether in order to remove excess secretions, allowing a few moments for drying. (3) elevate the foot by placing the heel on the corner of a chair seat in order to empty the veins. (4) stick two 6 inch strips of elastoplast 3 inches wide lengthwise along the lateral portions of the leg from the ankle to the calf. These need be used only when much edema is present or when an ulcer is so large that it makes a considerable portion of the bandage moist, thus favoring slipping and cutting into the skin. The strips serve to prevent creeping of the circular turns. Another method useful for preventing creeping of the skin is to overlap the spiral turns two-thirds instead of one third or one half of their width. They are applied slightly stretched. (5) The foot, ankle and leg are then covered in the order named with spiral turns of the elastic plaster. This is started to one side of the foot and brought across the dorsum to form a figure of 8 over the ankle (see Fig. 3) advanced spirally upward on the leg overlapping one-third to one half its width to a turn until the calf is reached. Here it is convenient to advance the bandage sharply upward in an

oblique direction in order to complete the highest turn which should be a half inch below the knee cap. It is then run downward again spirally so as to cover the remaining space with a few turns. In applying the plaster the entire ulcer if small enough should be included in one of the turns. This will avoid the cutting of ridges in the granulations by the edges of the plaster. The tension or pull exerted on each turn of the bandage as it is applied should be at least sufficient to stretch the material to the limit of its elasticity, preferably a little greater. With the material we use this will actually register six to eight pounds of linear pull on a spring scale. This expressed in pounds per square inch would be a much smaller figure.

In order to calculate the number of pounds of pressure exerted per square inch of skin surface, we employ a formula which was kindly furnished by Dean Fred J. Lewis of the School of Engineering of Vanderbilt University. Disregarding friction loss which would be overcome by the skin slipping freely over the subcutaneous tissues during application of the bandage, the formula is as follows:

Total Load = Unit pressure  $\times$  width  $\times$  diameter or

$$R = \frac{2P}{Wd}$$

$P$  = Recorded load in pounds  
 $R$  = pressure in pounds per square inch exerted by the bandage  
 $W$  = width of bandage in inches  
 $d$  = diameter of cylinder wrapped

Thus if a bandage having a width of 3 inches were applied with a 6 pound linear pull (without overlapping) to a portion of the leg having a diameter of 3 inches, we may obtain the pressure of the plaster on the surface by substituting in the formula as follows:

$$R = \frac{12}{3 \times 3} = \frac{12}{9} \text{ or } 1\frac{1}{3} \text{ pounds per square inch}$$

If each turn of the spiral bandage should be lapped over the last turn by one-half of its width this pressure would be doubled.

It is difficult to impress upon surgeons the necessity of applying the bandage tightly. They are usually afraid of "cutting off the circulation," yet the stagnant venous circulation is exactly what one must "cut off" in order to benefit the tissues. We have never heard of any harm resulting from a too tight

application of a bandage unless it be that temporary crease marks occurred from an uneven application of the turns. Rather than being retarded healing is hastened by sufficient pressure. When ulcers fail to improve it is nearly always due to the bandage being applied so loosely that it fails to contract to the reduced size of the leg as the edema subsides. For this reason we agree with Wright in saying that in treating patients with marked swelling of an extremity the initial elastic bandage should be replaced by a tighter one in about 4 or 5 days in order to take care of the great reduction of swelling which in such cases almost invariably occurs. If the extremity is not swollen at the time of the first dressing the initial bandage may be left on for the usual time.

Pain may occur for 4 or 5 hours after bandaging. This is usually not due to too much pressure but rather to the circulation readjusting its paths of flow. This pain is usually temporary and may be relieved by the usual sedatives. It is a good plan to provide a sedative the first night to insure rest for the patient, since he is not accustomed to the bandage and as Wright naively remarks "misses the ulcer." It is also necessary to tell the patient that he may go about his duties in the usual way and use his leg, for best results are obtained when the leg is used right along. In case any wound exudate works out through the meshes of the bandage, which is semi-porous, the patient may wash this off with neutral soap and water on a little gauze or a brush. Water will not damage the cloth in any way. After washing, the surface should be dried.

After the first change, it is usually sufficient to renew the bandage only once each 2 to 3 weeks, in fact best results are obtained by infrequent changes. At each re-dressing the elastic adhesive is cut along the side of the leg and foot opposite the ulcer and removed. Any pus underneath is gently sponged away with dry gauze but no other cleansing is done. Before re-application of the bandage the exact size of the ulcer is determined. This is done by tracing the exact size of the ulcer with ink on sterile transparent tissue and by transferring this to the history sheet as a permanent record (see

Fig. 4) If desired the exact area may easily be computed by a transfer to bond paper of known weight per square centimeter ( $x$ ) and by weighing the exact pattern which is then cut out by scissors. By one of these procedures all guess work is eliminated, for one may easily see with "his own eyes" what progress the wound is making either in healing or in breaking down.

It was through such simple quantitative studies that we have been led to adopt elastic adhesive strapping as the method of choice in the conservative treatment of superficial ulcerative conditions, especially of indolent ulcers of the legs.

The applications of the elastic bandage at stated intervals are kept up for one visit after the ulcer is seen to be completely healed. Following this the patient is told to bathe the leg including the ulcer site with a neutral soap and water to gently massage it with alcohol, to allow it to dry and to powder it with borated talcum or zinc stearate. He is also given an elastic cloth bandage of the "Ace" type to wrap around it for slight pressure. He is told to return immediately if any break in the skin should ever occur.

*Use of a pressure pad over small deep ulcers.* In a few instances in which elastic adhesive was used on large ulcers healing has progressed until a small but deep crater like ulcer remained. After this stage the healing was very slow even though the ulcer measured only 5 to 6 millimeters in size. In such cases we feel that the reason why the epithelium does not grow in to cover the granulations promptly is evident. If the plaster is applied in the usual manner its under surface will be stretched from one edge to the other and will, therefore, be out of contact with the steep sides and deep base of the ulcer. A "dead space" at first filled with air and later with exudate will thus be formed. In order to obviate this the first layer of elastic adhesive is applied under a small amount of tension. Then a pad of gauze or sponge rubber of a size and shape suitable to fit down into the crater like depression is cut out with scissors. This is applied over the first layer of elastic plaster and is held firmly down into the depression by a second strip of elastic adhesive or a second turn of the band

age under considerable tension. Figure 5 shows the application of such a pad to the ankle. Healing which has been at a standstill has usually proceeded satisfactorily after such a pad is applied. This fact would seem further to show the advantage of pressure in promoting healing. The results of using the pressure pad in such cases are very striking.

*Local use of elastic adhesive straps.* In cases in which support of the veins of the leg is not necessary and in which only a small superficial ulcer is present a strip of elastic adhesive of a size suitable to cover the ulcer by a fair margin is cut with sterile scissors from the roll, stretched and firmly applied to the skin (Fig. 6). It should not completely surround the extremity. It is usually covered with a few layers of sterile gauze, held in contact by a gauze bandage. Healing under this in selected cases is very satisfactory.

#### CONTRA INDICATIONS

So far we have seen personally no cases except acute spreading infections and very deep ulcers in which elastic adhesive strapping seemed contra indicated. Wright has shown in the case of legs which have been damaged by long-standing venous congestion that "if gangrene supervenes as a result of senile or diabetic arteritis it is not the toes which are affected first but the skin of the leg in the usual ulcer sites. In these cases he feels that compression would be disastrous. Occasionally a compound fracture of the bones of the leg will result in a projecting knuckle of bone covered only with periosteum and skin. Over such an unprotected prominence, the pressure must be at a minimum in order to prevent ulceration. At first varicose or stocking eczema was thought to be a contra indication to compression but most of these cases while troublesome at best are less so with compression than with any other line of treatment. In case an eczema seems aggravated by the zinc oxide, one may change over for a time to a bandage impregnated with 5 per cent ichthyol or 5 per cent aluminum acetate as recommended by Wright. The important point to recognize is that elastic compression per se does not aggravate the average case of varicose eczema.

## ECONOMY OF THE DRESSING

The cost of any technique for the treatment of wounds should be considered as secondary to its therapeutic value. We find however, that elastic adhesive is very economical to use.

TABLE I—SHORTENING OF HEALING TIME ACCOMPLISHED BY ELASTIC ADHESIVE

	Time in years ulcer remained unhealed while under treatment by various remedies	Area in square centimeters at time elastic adhesive was started	Healing time in days from application of elastic adhesive	Cost of elastic adhesive treatment until ulcers healed
Ulcer 1	12	15 0	65	
Ulcer 2	20	41 5	51	
Ulcer 3	7	17 5	38	
Totals	29	74 0	154	\$13 56
Averages	9.6 years	24.7 cms	51.3 days	\$ 4.52

Table I illustrates its economy from the standpoint of time saved. These three ulcers taken at random from a series of many similar ones had been treated with many different dressings in various dispensaries including our own and failed to heal in an average time of 9.6 years. When subjected to elastic adhesive they healed in an average time of 51.3 days. The saving is obvious. The healing of the ulcer shown in Figure 1 is typical.

Ordinary dressings, by which we mean gauze, ointment, or antiseptic ones require the patient to return at least two and usually three times per week. Elastic adhesive requires only one application each 2 to 3 weeks. This means a great saving to the patient in work hours as well as to the staff physician, nurses, and other dispensary attendants. During treatment the patient is ambulatory, comfortable and able to work. The ulcer loses its foul odor in a few days and the patient is, therefore, no longer a problem to those with whom he associates at home or at work. Oftentimes a patient can retain a job if he has to lose only a morning each 2 weeks which he would be forced to lose if he had to come twice a week for dressings. So much for economy of work hours with elastic adhesive.

A computation of the money saved by this dressing shows rather striking figures. Some of these we briefly quote at the risk of ap-

pearing monetary in a medical paper. First, then, it is to be noted that the elastic adhesive technique requires no other article after the preliminary cleansing at the first visit than the bandage itself and a small dry gauze sponge or two at each dressing. Therefore the cleansing and antiseptic solutions, ointments, gauze, bandages and adhesive required for ordinary dressings are almost all saved through its use.

The chief economy in money is made possible through the relative infrequency of dressings required. To get at actual figures one visit in 2 weeks requires only one elastic adhesive bandage, one registration, and one transportation cost against four to six each of the latter two for a similar period with the usual gauze dressings.

At the average price we have paid for the elastic bandage the cost of treatment would be cut to one half by its use (\$5.55 compared to \$11.75 per week).

To be more specific the three old ulcers described in Table I would have required a total cost for dispensary treatment by the older methods in excess of seventeen hundred dollars in the 9.6 years during which they were treated without cure. With elastic adhesive, they were healed in an average time of 51.3 days, at an average cost of \$4.02. It is usually not necessary to keep this new dressing up for more than a short time in order to accomplish healing. However, even granting that it were, the annual saving over the older dressings would be about \$32 per ulcer. The average healing time of large ulcers we have shown to be about 51 days. At Vanderbilt, a hospital with 205 beds, the incidence of ulcer of the leg in the Out-Patient Department was 83 per year in 1933. Granting that this incidence was proportionately the same in this country at large in the various approved hospitals<sup>1</sup> having surgical clinics, and assuming that the ulcers would heal only as well by the older methods as usual the annual saving effected for these patients by elastic adhesive in the United States would be well in excess of three million dollars. This money would be saved for precisely the patients who are in the

<sup>1</sup> Hospitals approved for internships by the Council of Medical Education and Hospitals of the American Medical Association. J. Am. M. Ass. 1933 101 699

greatest need of funds. Furthermore a far greater saving would be accomplished for them by the removal of disability and loss of work hours directly attributable to this form of therapy.

#### PROPERTIES

The chief purpose of using a semipermeable elastic adhesive dressing is to obtain rapid firm healing of ulcerated surfaces. The following properties of the plaster contribute toward this purpose:

a. It is perfectly adhesive which provides the following advantages: Its firm adherence to the skin up to the granulations splints the wound putting the tissues at rest and preventing the rubbing off or injury of the delicate growing epithelium at the periphery of the wound—an occurrence so usual with other dressings. Its adherence seals the skin away from the ulcer base so that secretions from the wound will not moisten the unsterile skin and then run back to cause re-infection of the granulations. When the dressing is removed desquamated epithelium comes off with it leaving a clean skin and wound surface ready for the next application.

b. It is semipermeable. When the bandage is stretched a fit should be during its application the small spaces between the threads of the cloth are opened up. This permits the escape of excess secretions through it under slight pressure. The vacuum system so formed thus retains enough secretion at all times for healing under moist conditions to take place. This may be likened of a *covered drainage*.

c. It is permanently elastic. This property of elasticity which the plaster exerts continuously 24 hours a day accomplishes several important ends. It provides an excellent firm support for sin which collapses and ulcers thus preventing back pressure and stagnation and improving the nutrition of the part. It provides an "last" support for the tissues which stretches if the leg swells but which again contracts if it shrinks. Thus edema gradually subsides and by contraction of the swelling for the size of the wound is diminished. It intensifies the contraction to mention that careful observation that contractions are an important factor in the healing of wounds

even in tissues which are not swollen. This point will be discussed in a later report. It further provides a leveling or flattening influence both for the growing edge of the ulcer and for exuberant granulations. Lastly it provides a smooth immobile contact surface of gummy consistency allowing epithelial cells to grow evenly over the granulations.

d. It is bactericidal in effect. The number of organisms is usually rapidly reduced until sterility is reached. This is probably not due to any antiseptic quality of the plaster but to the conditions which it produces locally as follows: It seals the wound and prevents re-infection. It supports and compresses the veins thus producing a more active circulation to resist germ growth. It favors rapid epithelial growth and thus quickly reduces the size of the field in which bacteria may multiply.

e. It is waterproof. Since it is waterproof the patient may cleanse its outer surface with soap and water as often as it becomes soiled.

In using this bandage we must recall that in reality we are employing a material which is a "happy combination" of many past aids to ulcer healing. The virtues of the elastic stocking of the atherosclerotic advocated by Morton and Beck of Unna's paste of the paraffin method of treating ulcers, and of the use of gutta serena by Halsted—all are embodied in this one dressing and yet it seems to have none of their shortcomings or disadvantages.

The properties of the elastic plaster which we have enumerated seem to combine in quite an unusual manner to promote the comfort of the patient and the rapid healing of the wound.

Certainly it is that healing results with remarkable rapidity even in ulcers years old which have been treated and refractory to other forms of therapy. This is an everyday occurrence that the evidence is irrefutable.

#### RESULTS OF A TRIAL TREATMENT

This adhesive was first employed at Vanderbilt Hospital in the summer of 1911 and has been used constantly ever since. In the 3 years from July 1, 1911 to July 1, 1914, 111 cases were treated with the plaster of which

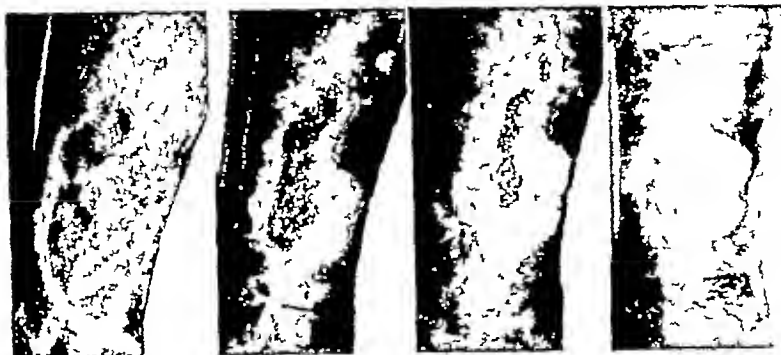


Fig. 1 Progressive healing in varicose ulcer treated by strapping with elastic adhesive.

90 were leg ulcers (i.e., ulcers on the legs, ankles, or feet) and 23 ulcers on various other parts of the body. Case abstracts are at hand in all but these would consume too much space if given here. Since almost all of the patients have been very co-operative in returning for observation, we believe that the results given are reliable. In only 1 case was a follow-up impossible. In this the ulcer had greatly decreased in size up to the time the patient failed to return.

In 3 cases of leg ulcer, or 3.3 per cent, the lesions improved but failed to heal in 12 months. In 4 more, or 4.4 per cent, the ulcers healed readily but recurrence occurred in a variable period either spontaneously (2 cases) or from some minor injury (2 cases). These recurrences were not serious and all healed promptly when the plaster was applied for a second short interval of time. All other patients of the 113 may be accounted for as cured.

In lieu of a large number of abstracts of case records we present herewith a few typical ones for the purpose of illustrating points of judgment which we regard important from the standpoint of treatment.

#### ABSTRACTS OF CASES ILLUSTRATING INDICATIONS FOR CONSERVATIVE TREATMENT AND RADICAL TREATMENT

CASE 1. M. W. Colored male of 67 years had a mechanical injury to his lower leg in 1925. This produced an ulcer and other ulcers have appeared and persisted. On physical examination the blood pressure was found to be 180/100. There was also a generalized arteriosclerosis and weak pulsations in

the dorsalis pedis arteries. When first seen on May 24, 1933, there were in all six ulcers on the anterior, lateral, and medial surfaces of the leg varying in size from 5 square centimeters to 0.75 square centimeters. Elastic adhesive was firmly but not tightly applied on May 24, 1933, and on June 10, 1933, all ulcers were found to be healed. The leg has been seen after a year and is still firmly healed.

This case is quoted to illustrate the point that elastic adhesive is indicated where ulcers are small, also that a bandage with moderate pressure may be used even though arteriosclerosis should be present and make radical treatment of the ulcers too great a risk.

CASE 2. W. W. Colored laborer aged 62. Varicose veins of left leg of 20 years' duration. Contusion of skin of left ankle 15 years before admission. Ulcer of medial surface of left ankle of 15 years' duration. Elastic adhesive was applied January 7, 1933. Five small deep or "pinch" grafts were applied on February 9, 1933. Elastic adhesive was used to complete healing April 7, 1933. The ulcer has remained healed nicely with an elastic cloth bandage to the present time. Figure 7 presents a similar case.

A minor surgical procedure like small deep (pinch) grafting may be used in conjunction with elastic adhesive in order to re-inforce the center of the healing area and so to make it stronger in resisting re-ulceration. This is well demonstrated by this case.

CASE 3. G. M. Negro truck driver of 64 years. Varicose veins had been present on both legs as long as he could recall. Thrombophlebitis of veins of right leg occurred in 1908. On admission to Dispensary March 26, 1928, the heart showed hypertrophy. At this time there was elicited a history of "brown" swelling present in both legs below the knees of several years' duration giving out the impression of non-filarial elephantiasis. An ulcer almost completely



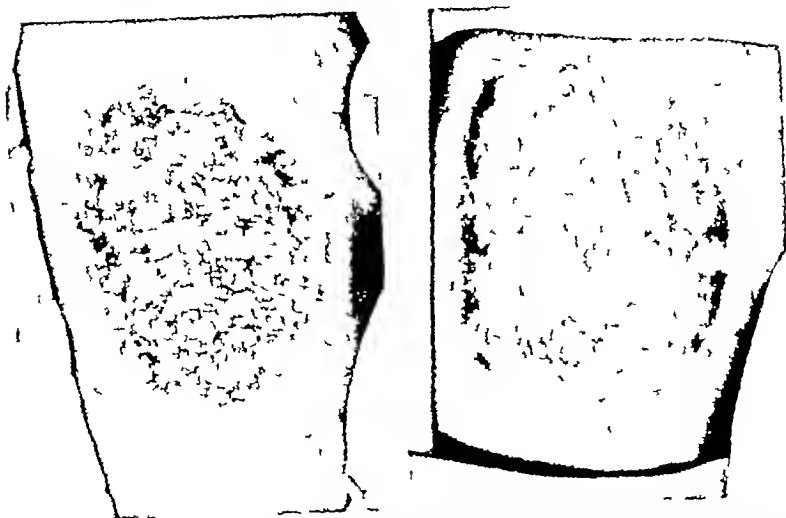


Fig 11 Treatment by excision and grafting Left, Site on thigh 14 days after removal of "sieve" graft. Islands are beginning to grow out. Right, Same area 42 days later showing firm healing with pliable skin.

confined to bed, the left leg swelled up and thrombophlebitis was diagnosed. Four months later he scratched his leg and an ulcer formed slightly above his internal malleolus. This enlarged until it was about 5 centimeters in diameter. It healed at times only to break down again. In December, 1932, he states that a "quack" doctor put on some medicine which caused tissue to slough out until the ulcer increased to twice its size. On admission February 9, 1933, a dirty shallow ulcer was seen in the region as described. It was oval in shape measuring approximately 6 by 8 centimeters (Fig 10). No varicosities were found. After a preliminary treatment for a few days with warm moist boric acid packs, elastic adhesive was applied from toes to knee. At this time the patient was advised to enter the hospital for total excision of the ulcer area followed by grafting. However, he could not make arrangements, and elastic adhesive was continued until April 14, 1933, at which time the ulcer had reached about one half its original size. On this date the patient entered the hospital. On April 18, 1933, a wide and deep excision of the ulcer bearing area was carried out thus leaving the muscles and some of the tendons bare in the wound. On April 27, 1933, a full thickness "sieve" graft cut to pattern was transplanted from the right upper thigh to the defect. It healed *per primam* and the photograph taken 2 months later shows both areas still stably healed with pliable pigmented skin. The donor site healed promptly with good skin as shown in Figure 11.

We abstract this case to show that while the method of elastic strapping may produce healing of a large ulcer over a joint it may not always be the procedure of choice. Here a full

thickness skin graft gave needed re-inforcement in a location frequently exposed to injury. In a young laboring man who had lost time because of several previous recurrences this was of great importance.

#### INDICATIONS FOR RADICAL TREATMENT

While in the great majority of cases conservative treatment by elastic adhesive has been found to produce unusually rapid healing it has failed to cure a few (3.3 per cent). Also a few of the seemingly cured cases (4.4 per cent) have recurred spontaneously or with minor injury or infection. On the other hand radical treatment i.e. by excision and full thickness grafting by the "sieve" method has resulted in cure in 100 per cent of 15 cases of large ulcer with no major recurrences. This radical method of treatment has been described in detail in two previous articles (2 and 3). It is our belief that radical treatment should be reserved for those patients who cannot be cured by conservative measures in a reasonable length of time. Although no absolute rules should govern individual cases our experience would seem to indicate that in the following types of ulcers conservative measures should yield at once to radical surgery through which alone permanent cure will be reasonably assured.





Fig. 3 Superficial granulating wound from burn of forearm almost entirely healed 8 days after stripping with elastic adhesive. Stain above indicates size of wound at time of first application.

encircled the right leg in its first and third and measured about 15 by 15 centimeters. This had been present for 3 years. The veins are not affected because of the history of thrombophlebitis. The ulcer on the right leg was treated regularly three times a week for 3 years and 1 month with various wet and dry dressings. At the end of this time it was very little smaller. Elastic adhesive was applied to the leg on February 10, 1935. Healing was complete on June 1, 1935. On September 3, one area broke down and formed an ulcer one-half centimeter in diameter but this quickly healed under elastic adhesive. Since then with an ordinary cloth pressure bandage there have been no recurrences.

Thus an ulcer of 6 years duration treated intensively at the hospital for 4 years without avail healed promptly without operation when elastic adhesive was applied. The cost of treatment to the patient for the 4 year period during which he was treated by wet and dry dressings is figured at a minimum of



Fig. 4 Illustrating the use of transparent adhesive tape in determining area of wound during the process of healing.



Fig. 5 Method of applying elastic dressing. First elevated on corner of chair. First turn over dorsum of foot. Second turn forming figure eight around ankle.

\$348.20. This does not include loss of time from work but merely the minimum dispensary registration fees and transportation. The total cost of elastic adhesive treatment including registration fees and transportation up to the time of healing was actually \$9.12. In the one case treatment cost the patient \$348.00 and the ulcer showed no tendency to heal. In the other his leg was healed before he had spent \$10.00.

CASE 4. L. W. Negro chauffeur aged 35 years, was admitted to hospital dispensary on April 5, 1936. He had primary syphilitic sore in 1916. Lesion was treated several years later at another hospital. He struck the left shin on concrete curb in 1929. This wound healed promptly but left lump at site. Pus was obtained on lancing this but the drainage wound then enlarged to form an ulcer which has been present ever since. On admission to hospital extensive complete circular scars are present the lower thirds of both legs with several open



Fig. 6 Application of pad cut to shape of depression on small, deep ulcers. Pad over first turn of plaster is covered with second turn for pressure.



Fig 6



Fig 7



Fig 9

Fig 6 Use of elastic adhesive strips on small ulcers

Fig 7 Ulcer in aged man which showed slow decrease in size under elastic adhesive A few small deep grafts applied in dispensary served to accomplish healing

Fig 9 Ulcer which after decrease to one third its original size in 2 months under elastic adhesive failed to heal further in 3 months Radical operative treatment is indicated

ulcers on the left (Fig 8) X-ray films showed slight irregular periosteal thickening of the left fibula Colon showed chronic ulcerative colitis Blood Wassermann report varied between negative, anticomplementary, and positive on different occasions Spinal fluid Wassermann was negative for 0.2 cubic centimeter of fluid, doubtful for 0.5 cubic centimeter of fluid He received intensive anti-luetic treatment and the usual dry, moist and ointment dressings to leg Meanwhile similar ulcers formed on his right leg He was admitted to the hospital but was discharged in a few days without improvement Dressings were continued along with anti-luetic treatment but new ulcers continued to form and the old ones would crust over at times only to break

down again When seen in the dispensary on May 24 1933, the patient presented a pitiable picture His face was drawn from loss of sleep and pain The latter resulted from multiple large and small ulcers extending over the larger part of the entire lower two-thirds of both legs (Fig 8) Both shoes were wet with pus which was running down from these ulcers He had been having moist dressings for several visits These were changed to elastic adhesive The pain was controlled by codeine for a few days and then spontaneously ceased The exudate which formed came out through the minute spaces in the plaster and was daily cleaned off at home with soap and water Gradually it became thicker and was released through a few small openings made with sterile



Fig 8 Multiple bilateral luetic ulcers Left before treatment right healed condition following use of elastic adhesive

1. Ulcers due to neoplasm (obvious but included for sake of completeness)

2. Ulcers in connection with elephantiasis

3. Very large ulcers surrounded and under laid by avascular scar tissue.

4. Ulcers in which conservative treatment would involve too great a time loss and too great a risk of further disability on account of recurrence (military and industrial group)

5. Ulcers which have failed to heal with conservative measures in 12 months

6. Ulcers in the region of joints which would heal with *scar contractures*.

7. Ulcers which after healing have spontaneously recurred or which have repeatedly recurred with minor injury

This list is not to be regarded as exhaustive. In the normal course of events the 3 patients whose ulcers we have reported above as failing to heal with elastic adhesive will be admitted to the hospital for radical treatment which, in our experience will almost certainly offer permanent healing. If however after a fair trial of elastic adhesive such patients refuse radical measures, usually by this time their ulcers are so much improved that the application of the plaster at 3 week intervals will suffice to keep their ulcers small and their legs very comfortable over an unlimited period of time. This no other dressing in our experience will accomplish.

One of these 3 patients who refused to enter the hospital had small deep or "pinch" grafts applied under local analgesia in the dispensary with the result that he is now healed (Fig 7). This may be regarded as a valuable semiradical procedure.

#### CONCLUSIONS

1. The cure of large ulcers especially of those on the lower extremities has become extremely important in modern times on account of their increasing incidence.

2. Valuable advances have recently been made in this field along both radical and conservative lines, the radical treatment consisting of complete excision and grafting the conservative of special dressings.

3. Experience with many large ulcers indicates that all no matter how extensive may be cured by treatment directed along one or

the other of these lines provided that the underlying cause or causes be discovered and eradicated.

4. In our estimation after a critical experimental and clinical study of its properties and mode of action elastic adhesive offers an excellent method of conservative treatment much superior to any other so far developed.

5. Elastic adhesive represents the culmination of an evolution in dressings used in the past for these cases. It combines in one preparation the desirable properties of the Unna's paste boot, elastic stocking, gutta percha tissue and ordinary adhesive yet seems to possess none of their disadvantages.

6. Success in the use of this dressing depends upon a preliminary treatment of underlying causes of ulceration followed by an exact technique in its application. If these are carried out it will be found to be extremely comfortable and economical.

7. Prompt healing resulted in 96.7 per cent of 90 chronic leg ulcers treated at Vanderbilt Hospital with elastic adhesive during 1933-1934. During the preceding 20 years a large proportion of such ulcers had shown no improvement with other dressings. All of the cases which failed to heal completely never theless showed definite improvement with this treatment.

8. While elastic adhesive is at present the conservative treatment of choice in ulcers it failed in this series to cure 3.3 per cent and furthermore some which had healed under it recurred (4.4 per cent). For these ulcers and a few other classes, which are enumerated radical treatment is indicated.

9. Radical surgery by wide excision and full thickness skin grafting by the sieve method have proved curative for all of 15 such cases in our hands.

10. If for economic reasons radical measures are not feasible, elastic adhesive will offer the best substitute in treatment.

#### BIBLIOGRAPHY

- DOUGLAS B. ANN SURG. 73 679
- Idem SURG. Gynec. & Obst. 930, 50 618
- Idem South M. J., 45 24 51
- NEWELL, L. T. J. TENN. M. ASS. 61 24 305
- WRIGHT, A. DUNCAN. Roy. Soc. Med. 990, 3 1032
- Idem Brit. M. J. 470, Dec. 1, p. 904
- Idem Brit. M. J. 91, Sept. 26, p. 50

## A STUDY OF THE RELATIONSHIP OF PREGNANCY TO DISEASE OF THE GALL BLADDER<sup>1</sup>

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THIS investigation\* is undertaken to standardize and co ordinate fundamental features in our consideration of a large series of cholecystic disease. Our analysis is concerned with the relationship of the onset of cholecystic symptoms to pregnancy and with the findings elicited by clinical and laboratory tests in the established affliction as compared to a limited series of partial controls.

Rovsing reported a series of 344 patients with cholecystic disease more than 80 per cent of whom were mothers. William Mayo reported 3 075 female patients, 90 per cent of whom were mothers and in whom symptoms referable to the gall bladder became apparent during pregnancy or soon after.

In our service at St. Francis Hospital, 500 patients were operated upon for cholecystitis, 78 per cent of whom had been pregnant.

In the last 500 cases of gall-bladder disease among women at the Elizabeth Steel Magee Hospital exactly 375 or 75 per cent, gave an average history of 4.64 gestations each. There appear 114 miscarriages and 34 abortions in the 375 parous cases, constituting 9 per cent of the total number of pregnancies.

The fact that gall-bladder disease is much more common among women than men indicates that there must be some condition incident to womanhood which is a contributing factor. If 75 per cent of the cases of gall-bladder disease followed pregnancy then some condition must occur which predisposes to disease of this organ.

Careful study of the history of many of these patients shows that symptoms of gall-bladder disturbance began during pregnancy or soon after, often in the puerperium. The symptoms may be only mild at first. Gas after meals and nausea and vomiting are the out-

standing symptoms in the history, they often precede the attacks of severe pain which accompany the presence of gall stones. In many of these patients careful study of the history will reveal, during the course of pregnancy, evidences of toxemia such as headache, vertigo, increased blood pressure, etc.

It is difficult to demonstrate that the liver function becomes impaired to such a degree that the character of the bile is changed or that the gall bladder becomes involved. There has been much discussion as to the part the liver plays in the toxemias of pregnancy and also in the so called eclamptic state. Many observers are convinced that, even in a normal pregnancy, the physiological processes of the liver are subjected to extra stress. It is doubtless true that when a pregnancy is complicated by an unusual degree of toxemia, and where all organs are burdened with an extra load incident to the added stress the liver, from its very nature is called upon to carry a heavy load. As yet, we know but little about the chemical or physical changes that occur and for that reason a clear understanding of the clinical history and symptomatology is important. A true correlation between our knowledge of the clinical side and what may be gleaned from the chemist or roentgenologist, so far as the functional and physical properties are concerned, may eventually lead to a better understanding of what goes on in the liver and bile passages during pregnancy, and may direct the institution of treatment which might prevent the more serious effects.

It would seem reasonable that under such circumstances the bile may not have its normal characteristics, that the gall bladder and ducts may be exposed to temporary changes secondary to chemical irritation or to infection as a result of lowered resistance. It would appear that in the large percentage of these cases permanent injury persists. Clinical experience teaches that many cases of gall-bladder disturbance are due to poor drainage of

\*This study of the relationship of pregnancy to disease of the gall bladder was undertaken with the hope that the clinical side of the problem might be correlated with the chemical and X-ray findings and in this way provide more substantial proof of such relationship. It has been made possible through generous aid from the Buhl Foundation of Pittsburgh and the co-operation among the departments of chemistry, gynecology and obstetrics and radiology.

<sup>1</sup>Compiled under the auspices of the Department of Gynecology and Obstetrics of the University of Pittsburgh. Biological Research of the School of Medicine, University of Pittsburgh, January 11, 1933. Read before the Society of

the gall bladder and in a considerable percentage, there is a definite constriction of the cystic duct which interferes with its normal emptying powers. Improper drainage leads to pain and reflex disturbance in the gastrointestinal tract.

The size of the liver indicates its importance in the general nutrition of the body. It has many functions but the principal physiological unit lies in the liver cells. In the opinion of leading physiologists. Much is known about the normal physiology of the liver in relation to the formation and composition of bile and progress has been made in the study of certain metabolic functions, such as the formation of urea and glycogen. There are other important metabolic processes which are still imperfectly understood, as, for example, its relation to the production of fibrinogen, to the oxidation of fats, and to the detoxication of organic poisons.

One of its most important functions is the disposal of waste products, such as the pigments, cholesterol, bile acids, lecithin etc. Experiments show that stimulation of the splanchnic nerve diminishes the flow of bile while section of the splanchnic branches may cause increased flow. These actions are explained by their effect on the blood flow through the liver. Since the secretion increases when the blood flow is increased and vice versa. It is believed that in this case no special secretory nerve fibers exist (Howell).

If the liver is subjected to extra stress, even under normal conditions, it is undoubtedly true that when the patient is handicapped by an excess of poisoning and the inability to withstand the usual strain injury to the biliary tract may occur. It therefore becomes necessary to include the consideration of the possibility of the persistence of such damage after delivery and that careful study and attention be given not only to the normal pregnancy so called, but more particularly to pregnancy in which there are signs of unusual toxemia. Infection, stasis, and changes in the cholesterol and calcium content of both bile and blood have all been suggested as etiological factors. Most observers agree that hypercholesterolemia occurs in pregnancy. The work of Aschoff and Barmeister seems to show that gall-bladder disease occurs in cer-

tain instances without signs of infection. Certain individuals are handicapped by poor eliminative power in the liver and during pregnancy when the fetal waste products are added, there undoubtedly ensue changes in both the chemical and physical qualities in the bile which lead to precipitation and predispose to stasis. Investigations by Pribrom lead him to conclude that during pregnancy the cholesterol content of the bile was reduced while that of the blood was increased. In the puerperium he came to the reverse conclusion, that cholesterol content of the bile was higher while that of the blood was lower. He concludes that increased concentration of bile in the gall bladder does predispose to cholesterol calculi. Hofbauer advances the opinion that hypercholesterolemia in pregnancy is due to insufficient action of the liver cells.

Cholesterol, a non-nitrogenous substance is a constant constituent of the bile, and it is not supposed to be formed in the liver but it is eliminated by the liver cells from the blood. It is regarded as far as its appearance in the bile is concerned as a waste product of cellular disintegration. Lecithin, fats, and nucleo albumin, as found in the bile, represent waste products derived either from the liver or the body at large. The mucilaginous character of the bile is due to the presence of mucin or a nucleo albumin and aside from the fact that it has to do with the viscosity of the bile little is known about it. What may happen to this particular constituent of the bile under various circumstances remains unknown (Howell).

Much stress has been placed upon the theory of stasis of the bile secondary to enlargement of the uterus with pressure upon the bile ducts. The experiments of Westphal strongly indicate that there is a direct disturbance to the function of the biliary ducts. It is his contention that the action of the gall bladder and its various ducts is dependent upon Ochi's sphincter which derives its nerve supply from the vagus nerve. In his experience stimulation of the vagus causes peristalsis of the gall bladder and the biliary passages, thus inducing drainage of bile. Increased stimulation caused sufficient spasm to prevent drainage with the consequent stasis. He calls the

condition a motor neurosis of the biliary passages in pregnancy and is of the opinion that it is a motility neurosis of the biliary passages caused by the increased tone of the vagus and feels that the hypercholesterolemia of pregnancy is responsible for the disturbances of the hormones of the vegetative nervous system.

Experiments by Bacmeister and Havers indicate that hypercholesterolemia in pregnant women is the result of retention of lipoids and is not due to the direct formation of cholesterol within the organism. A pathological condition of the bile itself, secondary to disturbed cell action of the liver, supplemented by periodic interference with drainage of the entire biliary system, would seem to invite disturbed conditions of the gall bladder. This is true especially if to these predisposing causes are added infections of the various types.

So far as the bile pigment is concerned, the simplest explanation, which is supported by recent work, is that the liver cells excrete the bile pigment that is brought to them by the blood just as the kidney cells remove the urea from the blood. On this view the amount of pigment excreted would vary proportionately with the volume of blood flow.

The relief from many symptoms upon the withdrawal of fats from the diet in certain cases is in line with the idea. It is a well known fact that the reduction of meats and fats to which Germany and the other central countries of Europe were subjected during the late war brought about a marked reduction in the number of cases of eclampsia. Couinaud and Clogne, in a careful summary of the work done in hepatic function during pregnancy, have called attention to the antitoxic function of the liver as an important factor, and conclude that in pregnancy the liver protects the maternal organism against itself by the destruction of poisons which result from protein dissimilation and also against poisons from the outside.

It seems reasonable that the various liver function tests, particularly that of Rosenthal supplemented by radiological study, may eventually assist in clearing up some of these doubtful points both with reference to the part the liver plays in the toxemias of pregnancy and the crippled state of the gall blad-

der. A few cases have been reported in which, by means of cholecystography, certain conclusions have been made but no large series in which simultaneous cholecystography and determination of hepatic function during the various stages of pregnancy have been carried out, has come to our attention. It would seem necessary to make a rather wide study of this important subject which involves a considerable number of cases, before any definite conclusions can be made.

It was for this reason that we have undertaken such a study and now have an opportunity to report on a series of 388 patients. There is little doubt that, outside of the state of pregnancy, the method of Graham and Cole gives uniform and constant findings except in unusual instances in which there may be either errors in technique or an unusual reaction of the gall bladder and ducts to some unexplained reaction of the sympathetic nervous system. The questions as to whether a given gall bladder may be somewhat enlarged or just when its emptying time is exactly normal from a physiological standpoint under various conditions, may still offer opportunity for further refinement on the part of the roentgenologist.

Dellepiane believes that in his experience few deviations from normal occur in the first 3 or 4 months of pregnancy but states that with the fifth month there begin to be manifested definite noteworthy modifications in the form and dimension of the cholecystic shadow, in its less intensity and more rapid disappearance of the opacity. He concludes that while modification of the place, form, and volume of the cholecystic shadow observed in pregnancy can be attributed to elements of a mechanical character, it is more difficult to understand deviations from the normal which do not seem to depend upon these facts. He suggests that the complexity of the problem makes further and more profound elucidation necessary.

With reference to the bromosulphalein test for liver function in pregnancy, there seems to be conclusive evidence that it is usually positive in the graver forms of toxemia, especially in eclampsia. Siegel, King, and D'Aprile all believe that the liver function

test in eclampsia seems to indicate the degree of liver involvement. Siegel believes that it is valuable in pre-eclamptic cases in classifying the degree of toxicity and reaction to treatment and also valuable in differentiating nephritic from pre-eclamptic and eclamptic toxemia.

Here again there would seem to be an opportunity for further study. If in the case of an eclamptic the dye retention is always high, it is reasonable to conclude that there is still doubt as to when a given amount of dye retention may be considered abnormal. Whether it may be relied upon in the study of mild toxemias, even as corroborative evidence, is perhaps yet to be decided.

We have 388 cases in the cholecystogram series representing pregnancy from the second month to term and the puerperium for the first 30 days. There was but one case out of the group of 388 who did not have at some time during her pregnancy symptoms referable to the biliary system—heartburn, gas and nausea and vomiting being the outstanding features. We also have 21 patients from the toxemic clinic and ward, 1 of whom with a nephritic toxemia, began convulsive seizures 80 minutes after the injection of the dye.

Dye retention is found to be increased in the toxemic group and in the pregnant group in the time in which the placenta is undergoing its greatest development and later when the fetus is assuming greatest growth and development. Fatty acid content of the blood stream in the toxemic group is distinctly elevated, lying at the extreme high level of normal. The fatty acid content of the blood stream in the pregnant group gradually rises, reaching the highest point at around the seventh month. The cholesterol values are within normal limits throughout the toxemic and pregnant groups with the exception of the cases in 2½ and 9½ months groups, and even here we would be very hesitant about calling these values significant or suggestive of any pathology. In the puerperal groups the sixth and seventh days alone are represented by more than 10 cases. Fatty acid content of the blood stream lies at the high level of normal. Cholesterol lies at the high level of normal on the seventh day but is within normal limits

on the sixth puerperal day. There is a slight increase in non-protein nitrogen in each instance. Urea content is normal. Sugar is elevated above most of the figures seen in various periods of the prenatal course. Dye retention is less than that seen in a non-pregnant group of cases.

Of the 388 pregnant and puerperal cases studied by roentgen-ray 289 had reports of some existing cholecystic abnormality. In the order of frequency the diagnoses made were enlargement in 173 cases, poor emptying in 48 cases, distortion in 30 cases, small gall bladder in 17 cases, cholelithiasis in 9 cases, and faint shadow, slow emptying, adhesions, and distention in 20 cases.

In conclusion, the studies in this series of cases are concerned with organs, the physiological and pathological functions of which are open to much elucidation. Our knowledge of the influence which the hepatic and cholecystic functions exert over the level of the various constituents of the circulating blood is in many respects pitifully meager. The attempt to correlate concentrations of the various blood constituents with definite disease processes without a logical respect for physiological variations of health and disease is likely to lead us far from the actual truth. On the other hand it is of importance to determine the range of physiological response to the demands of increased strain of life as compared to the strain of disease. We therefore, critically analyze our work from the standpoint of a group of known truths.

The basic and signal contributions of Mann and his co-workers demonstrate the tremendous reserve of the liver. The urea formation in the liver of dogs was not appreciably impaired when 80 per cent of the organ was removed.

The increased demands on the constitution of the female during gestation may so alter normal protein physiology that the liver and gall bladder are subjected to insults which prepare the fields for later hepatic and cholecystic disease. We would emphasize our findings as an expression of functional aberration just as the symptoms of nausea and vomiting, gas after eating and epigastric fullness, heartburn, eructations, and headache (in a so

called physiological gestation) are literally billboards of dysfunction

The use of intravenous sodium-tetraiodo-bromo phthalein dye must be taken with reserve as a measure of liver function. We should keep the fact in mind that we are injecting a foreign substance into the blood stream, that this substance was originally used by virtue of the physical property of casting a roentgen-ray shadow, and that it is not free of undesirable side effects and may be irritating perhaps to hepatic tissues. We have seen wide variations in excretory response in patients with known cholecystic and hepatic disease. However, the syndrome of a borderline low blood stream sugar, a blood urea content of 8 or below, a dye retention (with standardized dosage) of 1.4 per cent or above at the end of one-half hour after injection and 8 per cent or above at the end of one hour, and a blood stream fatty acid content on the high level of normal or above, indicates hepatic impairment. The concomitant finding of roentgen-ray and clinical evidence of cholecystic disease presages a stormy cholecystic postoperative course in such an individual. The wise surgeon will resort to pre-operative supportive measures designed to restore depleted carbohydrate reserves in these individuals. It is our experience that the administration of intravenous glucose to secure this result is a highly commendable measure.

To sum up, of 388 cases we find 56, or 15 per cent, with evidence of well established gall-bladder pathology. The etiology in these cases must have antedated the present pregnancy and consequently must have been due either to previous pregnancy, or to some other cause. The remaining cases may conceivably have originated in the present pregnancy. Of these, we find 44 per cent with the gall bladder definitely larger than normal. This percentage is more than twice as great as was found in an approximately similar number of patients who were not pregnant. It would seem that this change might possibly have some bearing on the frequent development of gall-bladder pathology after pregnancy since it was the predominating abnormality which we observed.

The relationship between this phenomenon and disease is not apparent from observations made so far. A possible explanation may be that the enlargement is due to stasis of bile in the gall bladder, and this conceivably might predispose to disease.

Our studies did not reveal a large percentage of cases with delayed emptying of the gall bladder, but we do not believe this would rule out stasis as a cause of the enlargement. There might be many explanations to account for this apparent discrepancy. For instance, the customary high fat meal used to test the emptying ability of the gall bladder would hardly be selected as the average meal of a pregnant woman and might give one an erroneous idea as to the every day state of affairs.

Undoubtedly, much more investigation needs to be done on this subject, but we offer the suggestion that the frequent enlargement of the gall bladder which we have noted may have some bearing on the final solution of this problem.

Dr G. W. Grier gives the following summary as a result of his review of the cases in this study.

The X-ray findings in this series of cases were compiled from the X-ray reports which were made at the time of the examinations over a period of 2½ years. The reports were rechecked just previous to the writing of this article and very few changes were made, although naturally at this later period the authors have had the benefit of 2 more years of experience in the work of cholecystography.

The reports were made without a knowledge of the clinical aspects of the case and without any pre-conceived ideas of what we should find. As a matter of fact, many of these cases were passed on by the roentgenologist without his knowing that they belonged to this series and no effort was made to keep tab on what the findings were as we went along.

The interpretations, therefore, were not biased in that respect, and we are confident that we did not read into the roentgenograms something we were looking for, since, as a matter of fact, we had no idea what we were looking for.



Summarized the findings are as follows

	No	Per cent
Normal gall bladder	5	38 1/2
Abnormal gall bladder shadow	80	54
No shadow	20	7 1/2
Abnormal		
	No.	Percentage of total
Enlarged gall bladder	72	44 2/3
Poor emptying gall bladder	48	27 1/2
Stones	9	5 1/2
Small contracted gall bladder	7	4 1/2
Deformity of gall bladder	30	18
Faint shadow	20	12 1/2
No shadow	20	12 1/2

We see at once that less than half the cases had a definitely normal gall bladder. Of those that were abnormal we might deduct those that had stones, deformities that could be attributed to adhesions, or were small and contracted indicating marked disease of the gall-bladder walls, since it seems that these must have been diseased before the beginning of the present pregnancy. I say this because it is probable that more than 9 months would be necessary to produce these lesions. If we accept this, then the present pregnancy could hardly be responsible for them.

However they may have been produced by previous pregnancies and a consultation of our records shows that of

9 cases of stones, 9 had previous pregnancy  
 7 cases of contracted gall bladder 9 had previous pregnancy  
 30 cases of deformed gall bladder had previous pregnancy

A total of 30 of 56 cases, therefore have had a previous pregnancy which of course, might have been the etiological factor in their gall bladder pathology. These 30 cases might be said to show direct and definite signs of pathology.

The remaining signs of enlargement, faint shadow and poor emptying might be considered debatable first as to degree since this is a question of judgment and second it might be questioned whether they are actually evidence of pathology at all. However the large percentage of cases showing these findings makes one hesitate to dismiss them as having no significance.

Of the pregnant women of this series 44 per cent had a demonstrable enlargement of the gall bladder which should call for some explanation.

As a check against these findings, I have examined the records of the Pittsburgh Diagnostic Clinic where no pregnant women have been examined. Out of 458 cholecystograms there were 90 that showed enlargement, a percentage of 19 1/2 per cent and there were 47 showing poor emptying, a percentage of 10 1/2 per cent.

While the percentage of those showing poor emptying is about the same it will be noted that the percentage of enlargement is very much greater in the case of pregnant women.

Poor emptying which was recognized in a much smaller percentage (12 per cent) but still a considerable number of cases, might be considered as a natural accompaniment of enlargement since it must result in the latter condition if it persists for some time.

Faint shadow which has been reported by Levyn as a characteristic finding in gall bladders of pregnant women was present in only 5 per cent of our cases.

The finding of failure of visualization of the gall bladder we have ignored entirely since there is always the possibility that this finding may be due to errors in technique. Naturally in this kind of a case, the errors in technique would be greater than normal, and many of these patients were unable to speak English or were of such a low order of intelligence that they could not appreciate directions. So we feel that it would not be fair to accept failure of visualization as having pathological significance.

Röntgen-ray studies of cholecystitis offer definite and helpful diagnostic adjuncts, but the roentgen-ray plate cannot take the place of cortical cells in the estimation of the pathologic status of these cases.

There is a demonstrable similarity between the functional blood stream expressions of aberration encountered in certain phases of pregnancy as compared with various degrees of cholecystic and hepatic pathology. From the higher incidence of gall-bladder disease in women who have borne children from a comparison of clinical symptomatology and the functional metabolic disturbances seen in cholecystic disease and in pregnancy we are led to the conclusion that the institution of measures directed toward the control of func-

tional disturbances in pregnancy might contribute to a lowering of gall-bladder disease. This statement is made in the face of the knowledge of the high regenerative power of hepatic tissue.

The great temporary relief experienced by patients with chronic gall-bladder disease by the administration of diets containing a maintenance protein, a low fat, and a high carbohydrate encourages the belief that much permanent injury to hepatic and cholecystic tissues may be obviated at its inception. If the correctness of these concepts may become fact, the sphere of the obstetrician's usefulness in the field of internal medicine will be greatly extended.

Every pregnant woman who shows evidence of toxemia, as manifested by persistent nausea, vomiting, gas after meals, etc., to an unusual degree should suggest to the physician or obstetrician that he should not be unmindful of the effect upon the biliary tract, and in the treatment should appreciate the additional responsibility in the prevention of permanent disease of this organ.

#### BIBLIOGRAPHY

- 1 ARSTAMIANZ. Zentralbl f Gynaek., 1926, No 51a
- 2 ASCHOFF, L. Wien Klin Wchnschr, 1911, No 24, 559
- 3 Idem. Med Klin., 1912, No 1, 4
- 4 Idem. Beitrage zur Frage des Cholesterinstoffwechsels und der Cholesterinausscheidung. Berl Klin. Wchnschr, 1913, 50 17
- 5 Idem. Klin Wchnschr, 1922, No 29, 1345
- 6 ASCHOFF and BACMEISTER. Die Cholelithiasis, 1909
- 7 AUTENREITH and FUNK. Ueber kolorimetrische Bestimmungsmethoden die Bestimmung des Gesamtcholesterins im Blut und in Organen. Muenchen med Wchnschr, 1913, 60 1243-1248
- 8 BACMEISTER. Beitr z. path Anat., 1908, 44 528
- 9 Idem. Untersuchungen ueber Cholesterinausscheidung in menschlichen Gallen. Biochem Ztschr, 1910, 26 223-230
- 10 BACMEISTER and HAVERS. Zur Physiologie und Pathologie des Cholesterinstoffwechsels. Deutsche med Wchnschr, 1914, 4 385-388
- 11 BAR, P., and DAUNAY, R. Variations et balance de la nutrition azotee pendant la gestation chez la chienne. Compt. rend. Soc de biol, 1905, 59 138-140
- 12 BENDA, R. Arch. f Gynaek., 1923, 116 506
- 13 Idem. Zentralbl f Gynaek., 1928, 52 1644
- 14 BENEDICT. J Biol Chem, 1927, 51 187
- 15 BLOOR, W R. Studies on blood fat. II. Fat absorption and blood lipoids. J Biol. Chem., 1915, 23 317
- 16 Idem. Fat assimilation. J Biol Chem, 1915, 24 447

- 17 BLOOR, W R., and KNUDSON, A. Cholesterol and cholesterol esters in human blood. J Biol Chem. 1917, 29 7
- 18 BLOOR, PELKIN, and ALLEN. J Biol. Chem., 1928, 52 191
- 19 BOLLMAN, J L., MANN, F C., and MAGATH, T B. Studies on the physiology of the liver. VIII. The effect of total removal of the liver on the formation of urea. Am J Physiol., 1924, 69 371
- 20 Idem. Studies on the physiology of the liver. III. Muscle glycogen following total removal of the liver. Am J Physiol, 1925, 74 238
- 21 BRITTON, S W. Neural and hormonal factors in bodily activity. The prepotency of medulladrenal influence in emotional hyperglycemia. Am J Physiol., 1928, 86 340
- 22 COLE, CIPHER, and GRAHAM. J Am M Ass., 1928, April 7
- 23 CORI, C F. The rate of glycogen formation in the liver during absorption of fructose and galactose. Proc. Soc Exper Biol & Med., 1926, 23 459
- 24 CORI, C F., and CORI, G T. The rate of excretion of galactose. Proc. Soc Exper Biol & Med., 1928, 25 406
- 25 CORLEY, R. C. Factors in metabolism of lactose. III. Galactose tolerance in the rabbit. The effect of simultaneous enteral administration of dextrose and levulose on galactose tolerance in rabbits. J Biol Chem, 1928, 76 31
- 26 COUTAUD, P., and CLOGNE, R. Liver functioning during pregnancy. Gynec. et Obst., 1923, 7 372-387
- 27 CRAINICIANU, A., and POPPER, M. L'insuffisances hépatique au cours de la grossesse. Presse méd., 1921, 29 424
- 28 CROSS, R C. Various liver function tests in pregnancy. Am. J Obst. & Gynec., 1929, 18 800-807
- 29 D'APRILE, F. Function tests with tetrachlorophenolphthalein, 22 cases. Arch. di farmacol. sper., 1928, 44 193-224
- 30 DELLEPIANE, G. Roentgen study of function of the liver in pregnancy. Ann di ostet., 1929, 51 1266-1314
- 31 FOLIN. J Biol. Chem., 1926, 67 357
- 32 FRUGYEST, J. Med Klin., 1927, No 48
- 33 GILBERT, A., and LEREBOULET, P. Sur la teneur en bilirubine du dérum sanguin dans la cholémie familiale avec lithuase biliaire. Compt. rend. Soc. de Biol., 1905, 57 971-973
- 34 GRAHAM, E. A. Functional liver tests. Surg., Gynec. & Obst., 1923, 36 348-354.
- 35 Idem. Visualizing of gall bladder by the sodium salt of tetraiodophenolphthalein. J Am M Ass., 1924, 82 1777-1778
- 36 Idem. Cholecystography, use of tetraiodophenolphthalein. J Am. M Ass., 1925, 84 1175-1177
- 37 Idem. Cholecystography, use of phenoltetraiodophthalein. J Am M Ass., 1926, 86 1899
- 38 Idem. Simultaneous cholecystography and tests of hepatic and renal functions by single new substance, sodium phenoltetraiodophthalein, preliminary report. J Am M Ass., 1926, 86 467-468
- 39 Idem. Present status of cholecystography and remarks on mechanism of emptying of gall bladder. Surg., Gynec. & Obst., 1927, 44 153-162
- 40 Idem. Simultaneous cholecystography and determination of hepatic function. J Am M Ass., 1928, 90 1111-1113
- 41 GRAHAM and COLE. J Am M Ass., 1924, 82 613-614.

- 42 HARTLEY, P. On the nature of fat contained in the liver and kidney and heart. *J Physiol* 90, 31 553
- 43 HEDMANN, E., and NICHOLSON, J. Wien klin Wochenschr 9 24 41
- 44 IDEM. Ueber den Lipidgehalt des Blutes normaler und Sch. anger Fressen sowie neugeborener Kinder. *Biochem Ztschr* 9 2, 43 47-55
- 45 IDEM. Wien klin Wochenschr 9 2, No. 48, 557
- 46 HISE, A. F. and WICKEN, A. The development of marked activity in ergosterol following ultraviolet irradiation. *Proc Soc Exper Biol & Med* 93 24 46
- 47 HORN, K. *J Ztschr f Geburtsh* 908, 63 300
- 48 IDEM. *Med Klin* 909, N 7 30
- 49 IDEM. Hepatopathy, relation to pathogenesis of ectopic. *Zentralbl f Gynæk* 913, 57 35-42
- 50 HORN, H. *Zentralbl f Gynæk* 9 3, 30 33
- 51 IDEM. Gall bladder disease in gynecological conditions, review of literature for 93. *Monatsschr f Geburtsh Gynæk* 913, 93 377-81
- 52 HOWELL, *Textbook of Physiology* 16 ed Phila delphia W B Saunders Co 930
- 53 JAMIESON, W. C. P. The function of the liver in urea formation from amino acids. *J Biol Chem* 9 5, 557
- 54 KIRK, W. T. E. L. and LEATHER, J. B. A preliminary note on the excretion of the fat in the liver in health and disease. *Proc Roy Soc Med* 1908-909, Path Sec 36
- 55 KIVO, L. L. Functions of the liver in toxicosis. *South M J* 492, 3 281, 283
- 56 KLINIKER. Un erschöpfte und Gedanken wider den Cholesterinstoff. *ebend Berl klin Wochenschr* 9 5, 30 520-5
- 57 KROEMER, A. Relationship bet een cholesterol and cholesterol esters in the blood during fat absorption. *J Biol Chem* 9 7, 5 537
- 58 LEATHER, J. B. and MERRILL-WICKES, L. M. The destruction of fatty acids in the liver. *J Physiol* 909, 38 Soc Proc 38
- 59 LERICHE, G. L. Les troubles de la grosse veine. *Lille* 9 4, 48
- 60 LEWIS, R. G. O'CONNOR, M. and BRILLWICKE, M. Chemical changes in the blood during fasting in the human subject. *Arch f Med* 1904, 38 353
- 61 LEVINE, S. A. BORDERS, G. and DICKER, C. L. Some changes in the chemical constituents of the blood following starvation with special reference to the development of hypoglycemia. *J Am M Ass* 914, 81 778
- 62 LIMA, C. W. and TOLAR, E. Effect of an exclusive diet diet on chemical constituents of the blood. *Proc Soc Exper Biol & Med* 909, 26 124
- 63 LINDEN, W. *Walter Ztschr f Geburtsh* 9 4, 74 819
- 64 LINDENBERG, G. and LINDENBERG, O. H. Influence des carbohydrates sur le fonctionnement du rein et la de de la grosse veine. *Compt rend Soc de biol* 905, 58 60-604
- 65 MARY, F. C. The liver in relation to carbohydrate metabolism. *T Am Am Physician* 9 5, 40 30
- 66 IDEM. Modified physiological processes following total removal of liver. *J Am M Ass* 9 5, 85 47
- 67 IDEM. Howell's Textbook of Physiology
- 68 MAX, and HIGGINS. Effect of pregnancy upon the capacity of the gall bladder. *Proc Soc Exper Biol & Med* 926-27 24 920-93
- 69 MARY, F. C. and MAGATH, T. B. Studies on the physiology of the liver. II. The effect of removal of liver on blood sugar level. *Arch Int Med* 912, 30 75
- 70 IDEM. III. The effect of the administration of glucose to the condition following total extirpation of the liver. *Arch Int Med* 922, 30 71
- 71 IDEM. IV. The effect of total removal of the liver after pancreatectomy on the blood sugar level. *Arch Int Med* 923, 3 197
- 72 IDEM. IV. The effect of removal on the blood sugar following total and partial removal of the liver. *Am J Physiol* 923, 63 403
- 73 MAYO, WILLIAM. Innocent gall stones. *myth J Am M Ass* 9 5, 5 on 214
- 74 MEHLHORN, P. D. Studies on total bile. VI. The influence of diet upon the output of cholesterol in the bile. *J Exper Med* 914, 40 5
- 75 MERRILL, J. W. Recent work on the etiology of gall stones. *Glasgow M J* 914, 81 106-1
- 76 MEXER, ERIC, and FRIEDMAN, H. O. Klinisch-pathologische Bewertung von Gallensteinerkrankungen an Leberbottel. *Berl klin Wochenschr* 9 5, 5 700-700
- 77 IDEM. 920-743
- 78 MERRILL, R. Liver in pregnancy. *Science med* 923, 28-30
- 79 Abstracted in *J Am M Ass* 9 5, 60 667
- 80 MERRILL, R. *Arch ges de med* 89, Nov 8 and 9, 82
- 81 MERRILL, J. Choleliths chroniques traités par entropie en injections intraveineuses. *Bull et ann Soc med de hôp de Par* 930, 44 600-604
- 82 MERRILL, P. E. Functions of the liver in pregnancy. *Vic med* 930, July 5, pp 77-77
- 83 MERRILL, J. Zur Kenntnis der Bedeutung des Fettes und seiner Komponenten fuer den Stoffwechsel. *Arch f path Anat Physiol* 889, 80 70
- 84 IDEM. Zur Lehre von der Resorption, Bildung und Abgabe der Fett im Thierkörper. *Arch f path Anat Physiol* 884, 95 407
- 85 MERRILL, J. and FRIEDMAN, H. Ueber die Resorption der Nahrungsfette und der wechselnden Fettgehalt des Blutes nach Unterbindung des Duod. Thoracicus. *Physiol Centralbl* 904, 3 297
- 86 MERRILL, J. and ROSENBERG, A. Zur Lehre von der Resorption im Darm, nach Unterbindung des mes. Lymph (chylif) ductal beim Menschen. *Arch f path Anat Physiol* 89 3, 30 424
- 87 NIKOLAI, L. Function of liver. *End of normal pregnancy*. *Arch f Gynæk* 1913, 52 25
- 88 OWEN, B. L. and KARR, W. G. The lipid partition in blood in health and in disease. *Arch Int Med* 9 5, 56 907
- 89 P. KAMOR, R. H. Lesions in the liver in pregnancy (in pre-eclampsia and eclampsia). *J Obst & Gynec Brit Emp* 912, 99 777-803
- 90 PETERS, J. P. and V. SARKIS, B. D. Quantitative Clinical Chemistry, pp 9-12. Baltimore W. B. Saunders and Wilkins Co 93
- 91 PETERS, S. J. S. Pathology of gall stones. *West Canada M J* 9 5, 300-307
- 92 PETERS, EDWIN. *Häblicher (Gießen, 1923)*
- 93 IDEM. *Zur Gewinnung von Blausäure aus Kalk* des Mutter. *Physon Reflexes*. *Klin Wochenschr* 1912, N 15, 700
- 94 IDEM. Zur Frage des Cholesterinstoffwechsels während der Schwangerschaft und im Wochenbett. *Arch f Gynæk* 923, 57 9

- 95 RABINOWITZ, I M Biochemical findings in a rare case of acute yellow atrophy of the liver with particular reference to the origin of urea in the body *J Biol Chem*, 1929, 83 333
- 96 ROSENHEIM O, and WEBSTER, A. The parent substances of vitamin D *Biochem J*, 1927, 21 389
- 97 ROSENTHAL, F Concentration and resorption of bile acids in A and B bil. *Ztschr f d ges exper Med*, 1931, 78 498-510
- 98 ROVERING T Studier over Galdestenenenes Patogenese *Hosp-Tid*, 1915, 8 249-271 Discussion, p 310-328
- 99 Idem Contribution to the symptomatology of biliary calculus *Hosp Tid*, 1901, 9 825-834
- 100 SANSUM, W D, and WOOLYATT, R T Studies on the theory of diabetes. VIII Timed intravenous injections of glucose at lower rates *J Biol Chem*, 1917, 30 155
- 101 SCHADE Die psychologische Chemie in der inneren Medizin, Dresden
- 102 SCHAEFER, WALTER. *Arch f Gynaec.*, 1932, 150 696-740
- 103 Idem Physiology and pathology of gall bladder in pregnancy, labor, and puerperium, roentgenologic study *Fortschr a d. Geb d Roentgenstrahlen*, 1933, 47 42-59
- 104 SIEGEL, I A Function of the liver in pregnancy *Am. J Obst & Gynec*, 1927, 14 300-312
- 105 SIVCLAIR, R. G The rôle of the phospholipids of the intestinal mucosa in fat absorption Additional data on the phospholipids of the liver and smooth and skeletal muscle *J Biol Chem*, 1920, 82 117
- 106 STADIE, W C, and VAN SLAKE, D D The effect of acute yellow atrophy on metabolism and on the composition of the liver *Arch Int. Med*, 1920, 25 693
- 107 STEPP, W Ueber den Cholesteringehalt des Blutserums bei Krankheiten *Muenchen med Wchnschr*, 1918, 65 781
- 108 THANNHAUSER, E J Ueber den Cholesternstoffwechsel. *Arch f klin Med*, 1922-1923, 141 290
- 109 THEIS, E R The lipid distribution in normal and abnormal liver tissues III The effect of lipid distribution in human liver *J Biol Chem*, 1929, 82 328
- 110 VAN HOOGENHUIZZE, C J C, and A TEN DOESSCHATE Onderzoekingen over de stofwisseling bij zwangere vrouwen *Nederl. Tijdschr v Verlosk en Gynaec*, 1911, 22 38-74
- 111 VAN SLAKE, D D The present significance of amino acids in physiology and pathology *Arch Int. Med*, 1927, 19 56
- 112 VON SCHROEDER, W Ueber die Bildungsstätte des Harnstoffs *Arch f exper Path u Pharmacol*, 1882, 15 364
- 113 WALTER, H, and WILLIENCOURT, J A Function of liver in pregnancy *Gynec. et Obst.*, 1928, 18 127
- 114 WESTPHAL, KARL. *Ztschr f klin Med*, 1923 vol 96
- 115 Idem Ueber Physiologie, Pathologie, und Therapie der Bewegungsvorgaenge der extrahepatischen Gallenwege *Klin Wchnschr* 1924, June 17, 1105
- 116 WESTPHAL, GLEICHMANN, and MANN *Ztschr f exper Med*, p 115 Berlin Julius Springer, 1931
- 117 WESTPHAL, HANNOVER, and SCHONDEBE. Einige Bemerkungen zur Physiologie der Extrahepatischen Gallenwege *Klin Wchnschr*, 1927, December 17, 2417-2419
- 118 WHITAKER, L R The mechanism of the gall bladder and its relation to cholelithiasis *J Am M Ass*, 1927, 88 1542-1548
- 119 WHITEHORN *J Biol Chem*, 1921, 45 449
- 120 WIDAL. *Klin Wchnschr*, 1923 June 11, 1114
- 121 WITGENSTEIN, A Zur Klinisch-diagnostischen Beurteilung des Zuckergehalts der Zerebrospinalflüssigkeit. *Deutsche med. Wchnschr*, 1923, 49 246
- 122 ZACH RAYMOND L. *Northwestern Med.*, 1930, 29 468-472

## PEPTIC ULCER

AN EXPERIMENTAL STUDY<sup>1</sup>

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THE etiology and pathogenesis of peptic ulcer has offered one of the most perplexing problems of modern medicine. In an endeavor to elicit the facts in ulcer causation an enormous literature has been built up about the ulcer problem.

## REVIEW OF LITERATURE

Reviews of this literature have been brought up to date from one period to another by a number of authors. MacCullum reviewed the earlier experiments which were primarily concerned with the production of mucosal defects. Later McCann (16) made a comprehensive review of the literature which dealt with the production of ulcers by toxic manifestations, by vascular occlusion on a bacteriological basis and finally on the basis of trophic and glandular disturbances (neurogenic theory). These authors finally concluded that, with the many types of experimental procedures employed the occurrence of ulcers was variable. Contradictory results were reported. Of the particular lesions that did develop the smaller ones healed spontaneously whereas those that were too large led to the death of the animal. The production of a true, chronic, indurated lesion was the exception and not the rule.

In 1913 Boldyreff introduced a new thought which was to become monumental in the history of experimental peptic ulcer. By means of animal experimentation he was able to show that the concentration of hydrochloric acid, as secreted by the stomach was from 0.5 per cent to 0.6 per cent hydrochloric acid. Normally this concentration was reduced from 0.15 per cent to 0.2 per cent by the saliva, ingested food mucous secretions of the stomach and reflux duodenal contents. Of these he believed the reflux duodenal contents, and more specifically the pancreatic juice, to be the most important factors.

Following the promulgation of this theory of the self regulation of the acidity of the

contents of the stomach, the problem of ulcer causation for the first time came to be attacked with a definite working hypothesis. Attention was now focused on the neutralizing influence of the digestive juices found in the duodenum. In an endeavor to evaluate the importance of any one or combination of these juices, multiple ingenious surgical procedures have been devised. But however fantastic or simple a procedure employed, the objective has always been the same, namely to exclude one or more of the duodenal contents from the upper gastro-intestinal tract. It was thought that when the normal neutralizing mechanism was removed in part or in its entirety the acid-pepsin fraction of the gastric juice would be permitted to exert its deleterious influence on the intestinal mucous membrane.

Any one of these methods could be classified under one of three groups:

1. Those dealing with pancreatic extirpation.
2. Those dealing with exclusion of the duodenum, with or without its digestive juices.
3. Those having as their only objective—biliary exclusion.

*Pancreatic exclusion.* The problem of excluding the external secretions of the pancreas has been approached by injecting substances to inhibit the flow of pancreatic juice, or by tying off or cannulating one or both pancreatic ducts as they enter the duodenum. Jona (16) injected extracts of decomposing animal tissues and noted the occurrence of gastric and duodenal ulcerations which he attributed to the inhibited secretion of saliva and pancreatic juice. To add additional evidence in favor of this theory he then tied the main or both of the pancreatic ducts in dogs and subsequently demonstrated duodenal and occasionally gastric ulcers (17).

Ivy (14) studied the incidence of ulcers in one thousand necropsies which included healthy dogs, parathyroidectomized dogs, dogs with ligated pancreatic ducts, and supra-renalectomized dogs. Of especial interest were

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the 24 dogs with ligated pancreatic ducts. Four of these revealed superficial erosions. One animal, whose pancreatic ducts had been ligated 5 months previously, showed a typical, deep, eroded, indurated ulcer in the first part of the duodenum.

Gallagher studied experimentally the possibility of intestinal clamps causing subsequent ulcer formation. The pressure applied by the clamps was carefully measured in various surgical procedures. Following the application of sufficient pressure, acute ulcers could be demonstrated at the line of insult. The acute lesions healed quickly with the formation of scar tissue and a moderate dilatation and thinning of the wall of the duodenum at the site of the healed lesion. In one group of animals the main pancreatic ducts were ligated. The traumatic ulcers in these animals showed a delayed healing time. This delay in healing was attributed to the partial removal of the normal alkalinizing mechanism and to the cachexia of the animals.

More recently Elman (8) and his associates have carefully studied the relation of pancreatic exclusion to ulcer causation. These workers first provided a means of collecting the total external secretion of the pancreas under sterile conditions. In the uncomplicated instances the animals died in 5 to 8 days with marked asthenia. At autopsy it was noted that the stomach was small and contracted, particularly in the pyloric region. The hyperemic mucous membrane was thrown into deep folds and showed small erosions or ulcerations. Another group of studies (6) were then made under the same conditions to show the neutralizing influence of pancreatic juice on the gastric acidity. Their conclusion confirmed the original observation of Boldyreff that the reduction of the gastric acidity is in part due to the reflux of the alkaline pancreatic juice into the stomach. With this as a working hypothesis another series (7) of animals were prepared and life maintained as long as possible by careful feeding and the daily administration of 500 cubic centimeters of Ringer's solution intraperitoneally. Spontaneous peptic ulcers were observed in 6 dogs that were kept alive and in good condition for 13 or more days.

Matthews and Dragstedt based their work on the same hypothesis, but employed a new method in constructing permanent pancreatic fistulas. By the daily administration of salt solution their animals were kept alive for longer periods. In these experiments one, or more, chronic ulcers were found in the duodenum near the anastomosis with the stomach.

As a control study for their experimental work on peptic ulcer, Berg and Jobling employed dogs with pancreatic fistulas. Nine animals were observed for periods ranging from 17 to 52 days, respectively. They were unable to demonstrate any lesions in the stomach or duodenum.

From these contradictory reports, it becomes at once obvious that pancreatic exclusion as a method of inducing experimental peptic ulcers is at its best still a problem.

*Duodenal exclusion.* Other workers interested in the experimentally induced ulcer have employed the second type of surgical procedure, namely, exclusion of the duodenum with or without its digestive juices. The titles of "Surgical Duodenal Drainage" and "The Short-circuiting of the Duodenal Contents" have been coined to identify this type of systematic manipulation.

Bickel, quoted by Exalto, was interested in the study of biliary and pancreatic secretions in dogs with gastro-enterostomies. The procedure consisted of performing a gastro-enterostomy, extirpating the duodenum, ligating the pylorus and then transplanting the common bile duct and pancreatic ducts into the skin. Four and one-half weeks later the animal died following the perforation of a postoperative jejunal ulcer.

Later, Exalto, interested in the occurrence of gastrojejunal ulcers following gastro-enterostomies noted that although these particular lesions had been observed frequently in man, their occurrence remained unexplained. Because no experimental attack had ever been made on this problem he undertook this particular investigation. He performed gastro-enterostomies on a series of 7 dogs. When the dogs recovered from these operations combined acid (50 cubic centimeters 1 per cent hydrochloric acid introduced by a stomach

tube) and meat feedings were instituted. Three came to be autopsied because of secondary complications at 36, 160 and 197 days, respectively. There were no gross ulcerations or microscopic evidence of inflammation. The 4 remaining were living and well at the end of 223 to 289 days and failed to show any evidence of gastro-intestinal ulceration. From this he concluded that gastro-intestinal ulceration could not be produced by doing a gastro-enterostomy and following with acid meat feedings.

Unable to induce postoperative ulceration by these procedures, Exalto then resorted to the Y form of gastro-enterostomy. Four such animals were given acid meat feedings after operation. The first dog was sacrificed on the twenty-ninth day after operation because of a mistaken diagnosis. An ulcer was found in the blind end of the jejunum near the anastomosis. The second dog because of anorexia, nausea, and vomiting was sacrificed on the fifty-eighth day. There was no evidence of inflammation or ulceration. The 2 remaining animals died of perforated jejunal ulcers on the seventy-first and seventy-third days, respectively.

In the ulcer free animal sacrificed on the fifty-eighth day bile was demonstrable in the stomach and intervening duodenal segment. To this presence of bile Exalto attributed a neutralizing influence which he believed prevented ulceration of the gastro-intestinal mucosa. He then devised a method whereby the bile could be prevented from entering the prospective areas of ulceration. Three animals were prepared so that the jejunum was anastomosed to the stomach, the pylorus excluded, and then the distal end of the isolated duodenal segment implanted into the cecum. The first two were fed the acid meat mixture after operation and died of perforated jejunal ulcers on the twenty-first and thirty-eighth days, respectively. At this point it was noted that the ulcers seem to develop prior to the acid meat feedings. In answer to this the third dog was fed a mixed diet after operation and died of a perforated jejunal ulcer on the thirty-ninth day after operation.

Later Hehrer with a different motive, studied experimental ulceration. His thought

was to induce a prolonged and intermittent closure of the pylorus and note the effect in ulcer causation. In 15 dogs, he ligated the common bile duct, performed a cholecystostomy destroyed the duct of Wirsung and then anastomosed the duct of Santorini into the lower ileum. Nine animals failed to reveal any gross changes in the stomach after 9 to 159 days. In the 6 other dogs, definite microscopic changes of inflammation, erosion or ulceration were demonstrated after 9 to 106 days after operation. These changes were attributed to a hypermotility and increased acidity.

More recently Mann and Williamson employed the same principles with a modified procedure in that the contents of the duodenum was drained into the terminal ileum. Mann and Williamson and subsequent workers have repeatedly observed the occurrence of peptic (jejunal) ulcers in a large percentage of animals prepared in this manner. Through the efforts and numerous valuable contributions of Mann and Williamson this type of surgical manipulation has become almost a standardized method of inducing peptic ulceration in the experimental animal.

**Biliary exclusion.** In attempting to solve this problem of ulcer causation there has been a third and significant group of workers, namely those interested in the relation of biliary exclusion to ulcer causation.

Whipple (31 a) was the first to note the occurrence of peptic ulcers following complete exclusion of bile. Primarily interested in the output of bile pigment he prepared a series of animals by first ligating the common bile duct and then suturing the open fundus of the gall bladder to the skin. In this study he incidentally noted a deep penetrating duodenal ulcer in one of the animals that came to autopsy on the thirty-fourth postoperative day.

Kaplanow, interested in the experimentally induced ulcers following biliary exclusion criticized the work of Whipple on the assumption that infection might ascend by way of the gall-bladder sinus. To obviate this objection, he first performed a cholecystonephrostomy and then at a second operation ligated and divided the common duct. After this

second operation the course of the animals was progressively downhill. They lost weight, refused food and developed tarry stools. When autopsied or sacrificed at the end of 2 or more weeks the frequency of duodenal ulcers was high. Of this series of 43 animals, typical duodenal ulceration was demonstrable in 17 (40 per cent).

The next report on the incidence of experimental peptic ulceration following biliary exclusion was made by Berg and Jobling. These workers effected the complete exclusion of bile after the method of Rous and McMaster. Twenty-three animals were studied and divided into three groups. The first group comprised the uncomplicated biliary fistulas, the second group the biliary fistulas followed by biliary obstruction and the last group those with biliary obstruction. Of this series, ulcers developed in 60 per cent of the animals. In this study it is interesting to note that the dogs with complete biliary obstruction developed ulcers just as did the dogs with either temporary or permanent drainage of bile.

That peptic ulcers do develop in animals with obstructive exclusion of bile, is substantiated by the reports of other workers. Malkoff, quoted by Bogoras, stated that, by ligating the common bile duct, gastric and duodenal ulcers could be subsequently observed. Simnitzky, also quoted by Bogoras, ligated the common bile duct in 5 dogs. In 3, ulcers were observed in the pylorus and duodenum.

Hosomi, working on plastic transplants into excised portions of the common bile duct incidentally noted that many animals at autopsy presented peptic ulcers. Then to study the pathogenesis of these ulcerations, he repeated his experiments on 15 animals. Homogeneous transplants from the carotid artery were sutured into surgically made defects of the common duct. Seven of these animals (46 per cent) revealed either mucosal erosions, submucosal hemorrhages or ulcerations in the stomach or duodenum. Careful postmortem studies revealed that in 2 animals there was a definite complete mechanical obstruction. In 3 animals there was a definite constriction of the biliary passage. From

these observations he concluded that complete or partial interference of the flow of bile into the duodenum was an important factor in the pathogenesis of these ulcerations.

Bollman and Mann, in studying the experimental control of ascites in a large number of dogs noted that many animals were lost to the original study because of the early development of perforated duodenal ulcers. Their operative work consisted of producing an acute mechanical biliary obstruction. In 64 animals, acute, subacute or chronic gastroduodenal ulcers developed in 5 to 295 days. Twenty-three other animals died in 22 to 195 days but failed to show any gross evidence of ulceration. It might be added however that of these 23 animals, the cause of death in 8 was attributed to gastrointestinal hemorrhages.

That the loss of bile *per se* plays a rôle in the experimental production of peptic ulcers is further suggested by the work of Weiss and Hubster. A series of experiments was carried out in an attempt to discover the cause of gastroduodenal ulcer. In one group of animals the gall bladder was anastomosed to the ileum 30 to 40 centimeters beyond the cecum. Their thought was that there would not be a disturbance of the calcium metabolism such as would follow the complete external loss of bile. There followed an acute inflammation of the antral and duodenal mucosa interpreted as signifying a pre-ulcerous stage.

Pausing at this point to rationalize on the mentioned contributions to the problem of ulcer causation, certain deductions seem inevitable: (1) that pancreatic exclusion as a means of inducing experimental peptic ulceration is as stated still a problem, (2) that by short circuiting the duodenal contents to the lower bowel, peptic ulceration will follow in a large majority of instances, (3) that when there is a complete exclusion of bile from the entire, or at least the upper intestinal tract, peptic ulcers occur in a large majority of these animals.

That ulcers may be produced experimentally by either shortcircuiting the duodenal contents or effecting biliary exclusion the question arises "Why do peptic ulcers develop in these animals?" The answer to this



question may lie in the proper analysis of the distorted physiology following these operative procedures. In a consideration of the short circuiting method, the following changes are to be considered.

1 That appreciable trauma is inflicted on the gastro-intestinal mucosa is unquestionable. This is especially true where mechanical clamps are used. Attempts to evaluate the importance of this factor have been made by Gallagher, Exalto and others. The conclusions derived in each instance are not only confirmatory of one another but indicate that acute traumatic lesions inflicted on the normal gastro-intestinal mucosa heal rapidly usually within 10 days.

2 By dividing the stomach at or just proximal to the pyloric sphincter the normal sphincter mechanism is either interfered with or completely destroyed. That the normal function of the pylorus with its sphincter is disturbed in the ulcer patient is well appreciated by many clinicians. Some clinicians (11) feel so strongly about this particular disturbance as to say "When we can effect a dumping stomach in the ulcer patient we shall have found, or can find, the cure for ulcer disease." This same point has been equally well appreciated by many surgeons. Innumerable gastro-enterostomies have been performed on ulcer patients in hope of providing a means for the rapid emptying of the stomach. The questions now arise: How is this disturbance of the normal pyloric mechanism brought about in the ulcer patient? What relation does the extirpation or impaired function of the pyloric mechanism bear to the production of the experimental ulcer? At present these questions remain unanswered not only because of our inadequate knowledge of the normal pyloric mechanism, but also because of the etiological factors instrumental in producing peptic ulcer disease.

In the animals subjected to this shortcircuiting operation not only is the function of the sphincter mechanism impaired but by joining the jejunum to the stomach by an end to-end suture the lumen at the site of the anastomosis is appreciably narrowed. Further this narrowed lumen lies just distal to the powerful musculature of the pyloric antrum.

As a consequence of this distorted arrangement at the gastro-intestinal junction, the acid gastric chyme is forcibly ejected by the powerful antrum through the narrow outlet of the stomach into a more vulnerable region of the small intestine. Mann appreciated this fact and stated that he believed this to be one of the factors operative in producing ulcers in these animals. More recently however it has been demonstrated (15, 24) that when the muscular pylorus was resected and a wide anastomosis made between the stomach and jejunum the incidence of ulcers was equally high. This suggests that even when the motor drive effect is dissipated, ulcers continue to occur due to other factors.

Another end result of the shortcircuiting operation is that the jejunal mucosa is brought into direct contact with the gastric juice. In this connection Ivy and Fauley (15) have demonstrated that the jejunal mucosa is more susceptible than the duodenal mucosa to the deleterious influence of the gastric juice. That this fact alone is insufficient to account for the occurrence of ulcers in these animals can readily be appreciated by again referring to the work of Exalto. Exalto in his first approach to this problem, performed gastro-jejunoanastomies on normal dogs and then gave acid meat feedings. He never was able to demonstrate the occurrence of either gastro-jejunal or jejunal ulcerations.

As mentioned the tenor of the work on duodenal exclusion has been that the acid of the gastric juice not being neutralized by regurgitated duodenal contents, gives rise to ulcerations in the unprotected mucosa. That the acid pepsin fraction of the gastric juice is of great importance in the production of peptic ulcers must be conceded because of the tremendous amount of clinical and experimental evidence adduced in its favor. That it is not of paramount importance is being appreciated more each day by modern clinicians. It is more important to note that its actual occurrence in the experimental animal is becoming questionable in the light of recent investigations. That the variations in gastric acidity do not depend on the regurgitation of alkaline duodenal contents is suggested by the works of Berg and Jobling, MacLean and

Griffiths, McCann (25), Yesko, Ivy (15), and others

Finally the last change to be considered is the actual loss of the digestive juices of the duodenum to the upper intestinal tract. This loss comprises that of three digestive juices, the secretions of the duodenal mucosa, the bile and the pancreatic juice. Because of the technical difficulties encountered in attempting to isolate or exclude the secretions of the duodenal mucous membrane, we are unable at the present time to account for the rôle played by them in digestion or the significance of their loss in the experimental animal. That the loss of pancreatic juice questionably leads to experimental ulceration has been referred to above. In the ultimate analysis then of this shortcircuiting procedure it appears that the factor of paramount importance is the loss of bile to the upper intestinal tract.

That the loss of bile is so instrumental in inducing experimental ulcerations is readily appreciated from the work done on biliary exclusion. The particular method used in excluding the bile appears to be of minor importance. Whether the flow is obstructed, excluded to the exterior, drained into other viscera, or lost to the lower intestinal tract, the results are the same.

#### STATEMENT OF THE PROBLEM

The purpose of this study was to show that the loss of bile was of paramount importance in inducing experimental ulceration. The plan was to collect externally the bile as secreted by the liver and then to feed back to animal the bile that had been collected. The animals were then studied for the development of ulcers. To make the study comprehensive and in addition to try to determine whether the changes induced experimentally are comparable to the changes observed in man, all phases of this work were supplemented by careful histological studies.

#### MATERIALS AND METHODS

Three groups of animals were studied. The first group consisted of 2 normal dogs sacrificed to act as control studies. The second group consisted of 5 animals with complete external biliary fistulas. The fistulas were

prepared after a modified Rous-McMaster procedure under drop ether anesthesia and with aseptic surgical technique. The bile as secreted by the liver was collected externally in a sterile condom but was not fed back to the animals. In the third group of 3 dogs, the collected bile was fed back to the animals after being mixed with the laboratory stock diet.

In every animal when the condition became poor it was sacrificed to insure fresh material for microscopic study. Pieces of tissue were taken from all portions of the stomach, duodenum, jejunum and liver. The tissues from the stomach, duodenum, and jejunum were fixed in alcohol and prepared for staining with muchematein, hematoxylin and eosin and van Gieson's stain. The blocks of liver tissue were fixed according to routine methods in Zenker's solution and formalin and prepared for staining with hematoxylin and eosin, van Gieson's stain and a modified Hervey-heimer's stain for fat.

#### RESULTS OF EXPERIMENTS AND OBSERVATIONS

In the following pages are abstracted protocols of the animals used in this work. Following each record the observations made from histological studies are given.

##### *Normal (Control) Animals*

*Dog Normal No. 1* Medium sized, healthy, male mongrel. After a large feeding of chopped meat, food was withheld for exactly 24 hours and then the animal was sacrificed. At autopsy the abdominal viscera were grossly clean and normal. Microscopic studies revealed a normal distribution of glandular structures. In the muchematein stained section all of the mucous secreting cells were packed with deep blue staining granules. The nuclei appeared to be flattened against the basal border of the cells. On the surface of the entire gastric mucosa there was a film of mucin.

*Dog Normal No. 2* Small, active, male mongrel. This animal was given a large feeding of meat early in the morning and again early in the afternoon. The purpose was to study the cells after they were exhausted by physiological digestion. In comparison with the previous animal the chief changes were noted in the muchematein preparations. In these sections the mucous secreting cells presented the aggregation of deep blue granules only in the distal theca of the cells. The nuclei were large, ovoid, and occupied a more central position. The intermediate zone presented only a few lightly stained granules.

The surface of the mucosa was covered by a thin film of mucus.

#### *Biliary Fistula Dogs Without Bil. Feeds 12*

**Dog V 4-4.** Medium sized, brown and white mongrel weighing 16.8 kilograms. Complete external biliary fistula was made. Recovery after operation was uneventful and animal remained in good condition for 4 days with fair appetite and free drainage of bile. Thereafter condition was progressively down hill and drainage of bile became less to complete cessation by the eighth day. It was sacrificed on eighth day.

**Autopsy.** Weight 13.6 kilograms. Diffuse seropurulent exudate in peritoneal cavity. The only suggestive pathological areas were limited to the duodenum. Mucosa was reddened in large plaque-like areas suggesting an incipient duodenitis.

**Microscopic examinations.** The histological findings were practically identical to the findings in dog N 5-4 so that a single description will suffice for both animals.

**Dog N 5-4.** Medium sized tan female mongrel weighing 2.3 kilograms. Complete external biliary fistula was made. Immediate postoperative course was uneventful. Drainage of bile was free but animal refused all food after the first day. Condition was rapidly down hill and it was sacrificed on the eighth day.

**Autopsy.** Dog weighed 6.4 kilograms. The peritoneal cavity was grossly clean. The pathological area was limited to the pylorus along the greater curvature. Here there were small areas of reddish brown color suggesting petechial mucosal hemorrhages.

**Microscopic examinations.** No changes were noted in the cardiac and fundic gland regions. In the pyloric glands beginning inflammatory and degenerative changes were noted. These changes were limited to the superficial layers of the mucosa and occupied discrete areas of about 1 millimeter diameter. The margins of these altered zones gradually blended into the normal glandular mucosa. The characteristics of these pathological areas are the presence of an inflammatory exudate loss of the surface epithelium, destruction of the gland neck epithelium and occasional cystic dilatation of the gland necks. These changes were best seen in the hematoxylin and eosin stained sections as illustrated in Figure 1. In comparable sections stained with mucicarmum it was interesting to note that regardless of how much of the cell cytoplasm had been destroyed the remaining portion took on the characteristic deep blue staining reaction.

Paralleling these alterations in the pylorus, similar changes were noted in the mucosa of the duodenum. In the duodenum, however, the presence of a surface inflammatory exudate was not as constant as in the pylorus. The surface destruction also differed in that the changes varied from mere loss of covering epithelium to complete erosion and loss of the villi. The changes in the jejunum were identical but pro-

cent to less marked degree. These changes are also best demonstrated with hematoxylin and eosin staining as illustrated in Figure 2.

The only discernible change in the liver was a fatty degeneration of the hepatic cells lying about the central vein of each lobule.

**Dog V 6-4.** Large tan, female mongrel weighing 23.1 kilograms. Complete external biliary fistula was made. For 3 days, the condition of the animal remained good, ate with a fair appetite and there was free drainage of bile. Beginning with the fourth postoperative day her appetite became poor, drainage of bile scanty and the course progressively down hill. It was sacrificed on the thirteenth day because of the poor condition.

**Autopsy.** The peritoneal cavity was clean and the drainage tube was well walled off by omentum. While examining the liver, right sided subdiaphragmatic abscess was broken into. The liver in this region was deeply injected and edematous. In the mucous membrane of the pylorus there were small punctate areas of brownish discoloration again suggesting petechial hemorrhages. The mucosa of the duodenum and jejunum were diffusely reddened. On the posterior wall on the first inch of the duodenum were four small (one-half centimeter) superficial erosions.

**Microscopic examinations.** No changes are noted in the cardiac, fundic and pyloric gland regions. Esophageal findings were in the duodenum. In the superficially eroded areas described above there was almost complete destruction of the mucosa. The intestinal villi were entirely destroyed. The simple tubular gland portion revealed marked interstitial round cell infiltration with varying degrees of involvement. In some sections only the most superficial portions of the glands were eroded whereas in other sections (Fig. 3) almost the entire glandular layer was destroyed. In the Brunner gland region there was a dilatation of secreting acini and collecting holes. This dilatation ranged from almost normal appearing acini to almost unbelievable proportions as illustrated in Figure 3. In the mucoschnetic preparations any remaining portion of cell cytoplasm (of mucus secreting cells) took on the characteristic deep blue staining reaction. The remaining non-eroded portions of the duodenum revealed microscopic evidence of low grade duodenitis as described and illustrated under Dog N 5-4. In the jejunum similar but less marked changes were demonstrable.

Fatty changes in the liver were similar to the changes described for Dog N 5-4.

**Dog N 9-4.** Small, tan, long haired, female mongrel weighing 3 kilograms. A complete external biliary fistula was made and drainage of the bile as free and the animal felt well for 3 days. Thereafter appetite steadily diminished. Course as progressively down hill and dog was sacrificed on fifteenth day after the drainage tube was pulled out.

**Autopsy.** Dog weighed 7.7 kilograms. The peritoneal cavity was clean except for several small

periductal abscesses near the hilus of the liver. Multiple pin-head-sized brownish spots were found in the pyloric mucosa. In the first part of the duodenum there were three small ulcers about one half centimeter in diameter. The ulcers were shallow with flat edges. The remainder of the duodenal and jejunal mucosa showed a diffuse reddening.

*Microscopic examinations* No changes were noted in the cardiac, fundic or pyloric regions. The chief findings were in the ulcerated areas of the duodenum. The lesions appeared active with sloping edges formed by the mucosa proper. The bases of the lesions were made up of an inflamed debris resting on the submucosa. The submucosa was infiltrated with round cells, appeared edematous, and seemed to bulge up into the base of the ulcer as illustrated in Figure 4. The remaining portions of the duodenum and jejunum revealed usual changes of duodenitis and jejunitis as referred to. The liver showed fatty changes as previously described.

*Dog No 2-4* A large, short-haired, tan female mongrel weighing 20.9 kilograms. Complete external biliary fistula was made. As in the other dogs this animal ate well at first. After the first few days the animal lost her appetite and her condition became poor. She was sacrificed on twenty-third day after operation.

*Autopsy* Dog weighed 13.6 kilograms. The peritoneal cavity was clean. Petechial areas of discoloration were noted in the pyloric antrum. In the duodenum and jejunum there was a diffuse reddening of the mucosa. Other than for a somewhat mottled appearance the liver appeared normal.

*Microscopic examinations* No changes were noted in the cardiac glands. The most interesting findings in this animal were confined to the fundic and pyloric gland regions. In the gland region of the fundus the pathological areas were patchy in distribution being separated from one another by normal mucosa. There was a loss of the covering epithelium and various degrees of destruction of the secreting tubules. In some places only the neck of the gland would be gone whereas in other places the entire secreting tubule would have been destroyed. In between the individual tubules there was an increased amount of interstitial tissue. The result of this was a distortion of the normal closely packed, palisade like arrangement of the fundus glands. These changes are illustrated in Figure 5.

The sections of the pyloric mucosa revealed a museum of gastric changes. The picture was so complete that the destructive process could be traced from beginning to end. The earliest changes have been described under dog No 5-4 and illustrated in Figures 1 and 2. The next stage consisted of a destruction of the gland neck epithelium while the fundus portion of the glands continued to present a normal appearance. At the same time the interstitial tissue appeared to be increased and infiltrated with round cells (Fig. 6).

In Figure 7 the destruction has progressed to involvement of the fundus portion of the glands. The

glandular tissue that had been destroyed was replaced by a loose inflamed tissue infiltrated with leucocytes, lymphocytes, and plasma cells. In many areas only a vestige of the gland neck was to be seen and the fundus portion of the gland was beginning to succumb to the destructive process.

In the final stage of destruction as illustrated in Figure 8, there was a complete loss of all the glandular structures. In some regions there remained only a vestige of the secreting acini. The mucosa was now replaced by a loose, amorphous tissue, diffusely infiltrated with round cells and plasma cells.

In examining sections comparable to those here mentioned but stained with muchematein it was noted that despite the amount of destruction that had taken place as long as there were any cytoplasmic remnants of the specific cells they took on the characteristic, deep blue staining reaction.

In the sections taken from the duodenum and jejunum there was a marked duodenitis and jejunitis. In the liver the usual fatty changes were noted.

#### *Biliary Fistula Dogs with Bile Feedings*

*Dog No 3-4* Large female mongrel weighing 23.6 kilograms. Complete external biliary fistula was made. This was the first animal to have bile feedings. About one half of the bile collected was fed back to the animal by means of a stomach tube. Between feedings she was permitted to eat at will. This plan, however, was not effective for after the first 3 days the animal refused all food and often had an emesis after the feeding of bile so that probably very little bile was retained. The condition of the animal became progressively worse and after the seventeenth day a purulent material replaced the secretion of bile. Animal was sacrificed on nineteenth day because of poor condition and biliary infection.

*Autopsy* Dog weighed 20.0 kilograms. The peritoneal cavity was clean. The extrahepatic biliary passages were dilated, injected, and edematous. When opened into there escaped an appreciable quantity of frank pus. The liver was diffusely reddened and presented a mottled appearance. The stomach appeared normal. On the anterior wall of the duodenum about 1 centimeter from the pylorus was an ulcer 1 by  $\frac{1}{2}$  centimeter in diameter. The adjacent duodenal mucosa was diffusely reddened.

*Microscopic examinations* No changes in gastric mucosa were noted. Essential findings were limited to ulceration in duodenum as illustrated in Figure 9. The base of the ulcer extended into the muscularis. Covering the base of the lesion was an amorphous mass of cellular debris. The adjacent submucosa was edematous and appeared friable. All layers of the duodenum revealed a round cell infiltration. The reddened mucosal areas adjacent to the ulcer revealed a low grade duodenitis. No noteworthy changes were demonstrable in the jejunum. Usual fatty changes were observed in the liver.

*Dog No 7-4* Large, young, tan female mongrel weighing 22.7 kilograms. Complete external biliary fistula was made. In this animal the plan of feeding

was changed. Twice daily the total secretion of bile for the 12 hour period previous was fed back after being mixed with the laboratory stock diet. For the first thirteen days after operation the animal appeared perfectly normal. On the thirteenth day there was evidence of biliary obstruction. The following day the abdomen was explored and a constricting ring located just proximal to the end of cannula. The extrahepatic ducts above this point were distended with white bile. The obstruction was released and drainage to the exterior was re-established. Convalescence was slow but progressive. In 5 days the animal pulled out the drainage tube and had to be re-operated upon to re-establish drainage. Convalescence was again slow but progressive. Ten days later the dog was again pulled out so that the animal was again explored to re-establish drainage. After this operation, the condition was only fair and in a few days became poor and the animal was sacrificed on the twenty-fourth day of biliary exclusion. The bile-food feedings were religiously carried out during this entire period.

*Autopsy.* Dog weighed 26.5 kilograms. The peritoneal cavity was filled with moderate amount of turbid yellow fluid. The omentum was thickened, injected, and edematous. The serosa of entire gastro-intestinal tract was deeply injected. Multiple perihaptic adhesions were noted. The mucosa of the stomach, duodenum, and jejunum presented a normal glistening appearance.

*Microscopic studies.* No pathological alterations were noted in stomach, duodenum, and jejunum. Superficial portions of liver revealed evidence of perihepatitis. The usual fatty changes were noted in the other sections of the liver.

*Dog N 144.* Medium sized, tan, female mongrel weighing 9.5 kilograms. Complete external biliary fistula was made. Bile-food feedings were given the same as in previous animal. The condition was good for first 8 days when the drainage tube was pulled out. Drainage was re-established by second operation. Three days after second operation the drainage of bile was replaced by foul smelling seropurulent material. From this point on the bile was obtained from other healthy dogs and the bile-food feedings were continued. For 7 days, the animal improved remarkably. After this her course was progressively down hill so that she was sacrificed after 3 weeks of biliary exclusion.

*Autopsy.* Dog weighed 5.0 kilograms. A diffuse purulent peritonitis was noted. The liver contained three walnut sized abscesses filled with thick pus. It was adherent to the lesser curvature of the stomach.

*Microscopic studies.* No alterations were noted in the gastric, duodenal, or jejunal mucosa. Fatty changes were again seen in the liver. Sections of liver from abscessed areas showed marked hepatitis.

#### DISCUSSION OF OBSERVATIONS

As previously mentioned the purpose of this study was to see if the ulceration in animals

with biliary exclusion could be prevented by feeding bile. From this work it is concluded that gastro-intestinal ulceration can be prevented in this experimental animal with biliary exclusion by the adequate feeding of fresh bile obtained from dogs.

Additional evidence supporting this contention is found in the incidental observations of other investigators working with some phase of biliary secretion. First is mentioned the work of Whipple (31 a) and his associates. As mentioned above these workers diverted the secretion of bile to the exterior by way of a gall bladder fistula. It was noted that the course of these animals was rapidly down hill and that the dogs soon died. As a result their first conclusion was that in order to make adequate studies on these animals it would be necessary to maintain them in as nearly a normal condition as possible. To attain this end they tried various feeding procedures and finally concluded that bile is essential in the life of these animals on a mixed diet.

More recently Puestow (37) made an experimental study of the discharge of bile into the duodenum. For the purposes of his study a number of animals were prepared surgically so that an isolated segment of the duodenum containing the orifice and intramural portion of the choledochus, was exposed on the abdominal wall. For the purposes of this paper it can be seen that his was simply another means of excluding all of the bile to the exterior. Following personal communications with this author (38) it was learned that several animals following these surgical procedures died rather suddenly. Necropsies revealed perforated peptic ulcers beyond the gastro-intestinal anastomosis. Other animals, however, remained in an apparently healthy condition for several years. These latter animals were frequently observed to lick bile from the fistulas and evidently ingested quite a large quantity of it.

The other side of this problem deals with the microscopic study of tissues involved in the disease picture. In this connection contributions by Konjetzny (30) and his associates are repeatedly referred to for a reason. First, these workers have pointed out what changes are to be looked for in peptic ulcer disease.

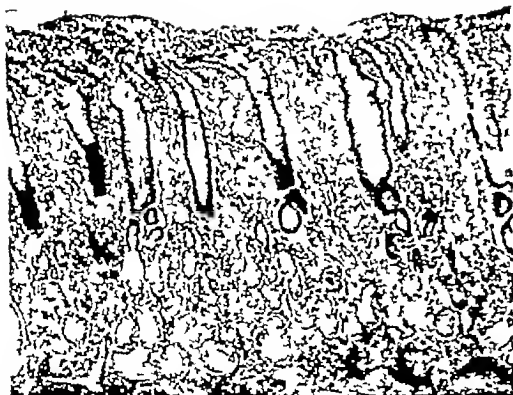


Fig 1 Dog No 5-4. Eight days of complete external drainage of bile. Section illustrates surface inflammatory exudate, loss of surface epithelium, beginning destruction of gland neck epithelium, and cyst dilatation of outer margin of a gland neck. Hematoxylin and eosin  $\times 50$



Fig 2 Dog No 5-4. Eight days of complete biliary exclusion. Hematoxylin and eosin stained section of first part of duodenum. This section illustrates surface exudate, loss of covering epithelium, and beginning erosion of tips of villi  $\times 50$

Second, a part of this problem has been not only to determine what associated pathological changes occur in these animals but to see if these findings are in any way comparable to the changes observed in man.

Gastritic changes in the pyloric region were described in dogs Nos 4-4, 5-4, and 2-4. The question arises why these changes are not observed with equal frequency in all portions of the stomach? Though this question must remain unanswered at present it is of interest that the same observation has been made for man by foreign investigators. It is only in the cases of a marked associated gastritis that changes can be observed elsewhere in the stomach i.e., in the fundus gland region. This fact applies equally well to this work as evidenced by the findings in dog No 2-4.

Another characteristic of the associated gastritis as observed in man and in these animals is the patchy distribution of the pathological areas. The importance of this is best appreciated by referring to the studies in dogs Nos 6-4 and 9-4. In these animals no alterations were noted in the gastric mucosa. This does not mean that such changes were not present but that the histological studies were inadequate. Either the pieces of tissue chosen were not large enough or were not selected from the proper regions of the mucosa.

Turning now to the alterations actually observed in these studies one is immediately

impressed with the marked similarity existing between these changes and the changes as observed in man. From the studies in dogs Nos 4-4, 5-4, and the less involved regions in dog No 2-4, it was noted that the destruction of the surface and neck epithelium of the pyloric glands constituted the earliest type of alteration in these glandular structures. Konjetzny has also described the gland neck epithelium as being first involved. In man however, the changes seem to occur less rapidly. Here the first manifestation is often a hyperchromatosis of the nuclei. Shortly thereafter the lumen of the gland necks becomes packed or plugged with an exudative mass, which subsequently may be followed by a loss or destruction of the gland neck epithelium.

Mention of this obstructing mass of exudative cells in the necks of these glands leads us to the next type of change to be noted, namely, the cystic dilatation of some of the glandular structures. As will be recalled, this was noted in the pyloric gland necks of dog No 5-4 and in Brunner's glands of the duodenum in dog No 6-4. The factor responsible for the dilatation of these glands is still unknown but a number of explanations have been offered. It has been suggested that the exudative mass accumulating in the necks of these glands causes an obstruction at the outlet of the glands and in turn is responsible for the dilatations noted. Another explana-



Fig. 3 Dog No. 64 Complete biliary ectasia for 3 days. Hematectomy and eosin stained section of first part of duodenum. Illustrating complete loss of intestinal villi, almost complete erosion of tubular glands, and dilatation of secreting acini and tubules of Brunner's glands.  $\times 50$



Fig. 4 Dog No. 64 Fifty days of external drainage of bile. Hematectomy and eosin stained section. Section illustrates active ulceration extending down to beginning of mucosa submucosa. Base of lesion filled with cellular debris.  $\times 50$

tion offered is that when the normal glandular structures undergo atrophy or are lost they are replaced by a new connective tissue. The new connective tissue laid down subsequently contracts and causes a stenosis or obliteration of the gland neck lumen.

Before dismissing the gastric changes, attention must be called to the alterations noted in the fundus mucosa of dog No. 34. In this connection there was noted an increase in the amount of interstitial tissue resulting in a forcible separation of the closely packed gland tubules. There was also a destruction or atrophy of the glandular cells manifested first in the necks of the glands and then in the fundus portions. Further in the regions where the process had progressed sufficiently to destroy entire tubules, there often could be seen one or more nests of from one to six parietal cells lying as vestiges in the path of the destructive process. These cells presented intact cell outlines and perfectly normal appearing nuclei.

This is of interest because Konjetany has made identical observations in his studies of gastritis in man. To explain this phenomena, Konjetany has attributed to the parietal cells a greater power of resistance to the destructive process which is responsible for these various alterations.

To introduce properly a discussion of the changes observed in the duodena of these ani-

mals, reference is made to a recent outstanding contribution of Puhl. This investigator made a detailed study of the development of gastric and duodenal ulcers in freshly resected human material. From these studies he has shown conclusively that the earliest stage of any ulcer begins in a minute erosion of the mucous membrane. He has also shown that by progressive development this minute erosion ultimately develops into the chronic, indurated lesion recognized clinically and pathologically as a peptic ulcer.

In this work it has been possible to trace an almost identical development of the ulcerous lesion. To relate more specifically the earliest stage or beginning of this lesion is manifested in dogs Nos. 44 and 54. In the sections taken from these animals there is chiefly a loss of covering epithelium of the villi. In some areas there is seen in addition a beginning erosion of the tips of the intestinal villi. In dog No. 64 this has progressed further to the point where in some areas the villi have completely disappeared and the erosive process is beginning to invade or already has invaded the layer of gland tubules. In animal No. 94 the glandular layer has been almost completely lost and the base of the lesion is now identified in close approximation to the muscularis mucosae. In dog No. 34 the lesion has progressed beyond the muscularis mucosae well into the submucosal layer and now is



Fig 5 Dog No 24. Twenty three days of complete external drainage of bile. Hematoxylin and eosin stained section of fundus glands. This section illustrates loss of surface epithelium, destructive changes in the tubules, and increased amount of interstitial tissue.  $\times 50$



Fig 6 Dog No 24. Complete biliary exclusion for 23 days. Hematoxylin and eosin stained section of pylorus. Illustrates loss of covering epithelium, destruction of gland neck epithelium with fairly well preserved fundus secreting acini.  $\times 50$

identified histologically as a peptic ulcer of the duodenum.

Up to this point little mention has been made of the conclusions derived from the study of the sections stained in the muchematein solution. It will be recalled that in the protocols of these animals attention was repeatedly directed to the fact that in the case of the mucus secreting cells as long as any portion of the cell cytoplasm remained it continued to give the characteristic staining reaction. This is histological confirmation of

the work of Whitlow that mucus laden and mucus covered cells are more resistant to acid-pepsin digestion than other cells. What appears to be more important, however, is the

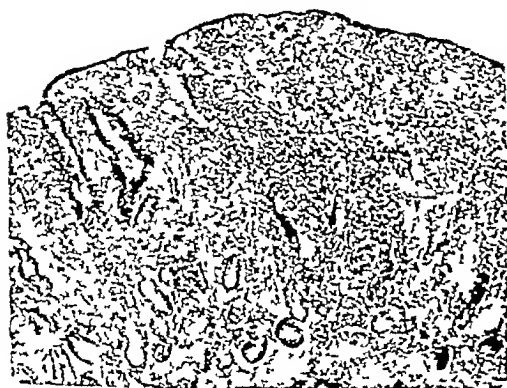


Fig 7 Dog No 24. Twenty three days of biliary exclusion. Hematoxylin and eosin stained section of pylorus. Section illustrates complete loss of surface and gland epithelium. Fundus portion of glands is undergoing destruction and in some areas the glands have already begun to disappear.  $\times 50$



Fig 8 Dog No 24. Hematoxylin and eosin stained section of pylorus. This section illustrates an almost complete loss of all the glandular structures. The mucosa has been replaced by a loose tissue densely infiltrated with round cells and resembling that which is found in inflamed areas.  $\times 68$



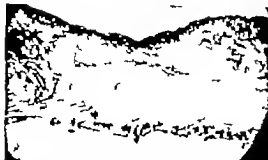


Fig. 9. Dog No. 24. Nineteen days of biliary exclusion with bile feedings. Duodenal ulcer stained with hematoxylin and eosin. Illustrates active lesion extending almost down to muscularis. Covering the base is an amorphous mass of debris.  $\times 9$ .

fact that, although these cells possess a natural power of protection they finally succumb to the influences of the destructive process.

In concluding, when a perspective view is taken of the changes occurring on both sides of the pyloric ring there remains another factor attracting attention. On the stomach side the changes are progressive and constitute chiefly a loss or atrophy of the gland structures. The mucosa, however, remains intact despite the fact that it becomes poorer in glandular elements. To describe this condition there has been coined the term "atrophic gastritis." Paralleling these alterations there are equally progressive changes occurring simultaneously on the intestinal side of the pyloric ring. Here the changes are manifested by a continual loss of tissue as described under the development of duodenal ulcers. At first the contrast in these changes may not seem important but, to the writer this fact affords an explanation why there is a preponderance of the duodenal lesion over the gastric lesion in peptic ulcer disease.

#### SUMMARY

The purpose of this study was to show that in dogs the loss of bile was not only of paramount importance in inducing experimental ulceration but that by the adequate feeding of fresh bile from dogs these changes could be prevented.

Two of the 10 animals were sacrificed for control studies. In 8 dogs there was effected a complete external drainage of bile. Five were

fed only the laboratory stock diet while the 3 remaining were fed the stock diet plus the bile that had been collected externally. In the dogs without bile feedings there developed not only peptic ulceration but the associated pathological changes of gastritis, duodenitis, and jejunitis. By incorporating fresh bile from dogs in the feedings, both peptic ulcers and the associated pathological changes could be prevented.

In the animals without bile feedings the associated changes of gastritis, duodenitis, and jejunitis were comparable histologically to the gastritis, duodenitis, and jejunitis associated with peptic ulcer disease in man.

#### BIBLIOGRAPHY

1. BIRD, B. N. and JOHNSON, J. W. Biliary and hepatic factors in peptic ulcers. *Arch Surg* 1930, 90: 977.
2. BUCKER, Ber. Klin. Wochenschr. 1900, No. 30.
3. BOGDANS, N. Ueber Cholezystoprostomie beim Menschen. *Arch. f. klin. Chir.* 1916, 34: 47.
4. BOLDRETT, W. The acid regulation of the acidity of the gastric contents and the real acidity of the gastric juice. *Quart. J. Exper. Physiol.* 1913, 8: 8.
5. BOLLMA, J. L. and MAYER, F. C. Peptic ulcer as experimental obstruction pancreas. *Arch. Surg.* 1931, 93: 21-30.
6. ELM, V. R. Probable influence of pancreatic juice on the regulation of gastric acidity. *Arch. Surg.* 1926, 101: 6-10.
7. ELMAN, R. and HARTMAN, A. F. Spontaneous peptic ulcers of the duodenum after continued loss of the total pancreatic juice. *Arch. Surg.* 1934, 98: 1090.
8. ELMA, R. and McCARDEN, J. M. On the collection of the entire external secretion of the pancreas under sterile conditions and the fatal effect of total loss of pancreatic juice. *J. Exper. Med.* 1927, 45: 50.
9. EVALTO, J. Ulcers jejuni, nach Gastroenterostomie. *Mitt. d. Grenzgeb. d. Med. Chir.* 1913, 17: 1.
10. GALLAGHER, W. J. Acute traumatic ulcers of the small intestine. *Arch. Surg.* 1927, 9: 680.
11. HOLMES, R. H. Personal communication.
12. HOPPER, G. W. and WINTER, G. H. Loc. cit. 3.
13. HONOW, K. Ueber das sogenannte peptische Geschwür des Magens und Duodenums beim Hund, das gewöhnlich der Choledochostomie entsteht. *Arch. f. path. Anat.*
14. IVE, A. C. Contributions to the physiology of the stomach. *Arch. Int. Med.* 1920, 5: 6.
15. IVE, A. C. and FULLEY, G. B. The chemistry of ulcers in the stomach and upper intestine. *Am. J. Surg.* 1923, 25: 53.
16. JONA, L. J. An experimental study of duodenal ulcer. *M. J. Australia* 1918, 9: 8, 104.
17. Iden. Further contribution to experimental study of duodenal ulcer. *M. J. Australia*, 1919, 9: 310.
18. KAPLAN, R. The experimental production of duodenal ulcers by exclusion of bile from the intestine. *Ann. Surg.* 1926, 83: 614.
19. KREMER, J. K. W. Ueber die Ursache des runden Magens geschwürs. *Mitt. d. Grenzgeb. d. Med. Chir.* 1914, 17: 670.

- 20 KONJETZKY, G E Die Entzündungen des Magen Handbuch der Speziellen pathologischen Anatomie und Histologie By Henke and Lubarsch Vol 4. Berlin Julius Springer, 1928, Gastritis, Duodenitis und Jejunitis in ihrer Bedeutung fuer den Chirurgen Beitr z klin Chir, 1931, 152 552, 581, Die Entzündliche Grundlage der typischen Geschwuersbildung im Magen und Duodenum. Ergebn. d inn Med u Kinderh, 1930, 37 184.
- 21 MACCULLUM, W G On the pathogenesis of chronic gastric ulcer Am Med, 1904, 8, 425
- 22 MACLEAN, and GRIFFITHS, W J The automatic regulation of gastric acidity J Physiol, 1928, 66 356
- 23 MANN F C, and WILLIAMSON Experimental production of peptic ulcers. Ann Surg, 1923, 77 409
- 24 MATTHEWS, W B, and DRAGSTEDT, L R The etiology of gastric and duodenal ulcer Surg, Gynec & Obst., 1932, 55 265
- 25 MCCANN, J C Studies on the control of the acidity of the gastric juice Am J Physiol, 1929, 89 483
- 26 Idem. Experimental peptic ulcer Arch Surg, 1929, 19 600
- 27 PUESTOW, C B The discharge of bile into the duodenum Arch Surg, 1931, 23 1013
- 28 Idem Personal communication
- 29 PUHL, H. Ueber die Entstehung und Entwicklung des Magen-Duodenal Geschwuers. Arch f klin Chir, 1930, 158 1-112
- 30 ROUS, P, and McMASTER. Sterile drainage of the intra abdominal ducts J Exper Med, 1923, 37 11
- 31 WEISS, A G, and HUBSTER, C The pathogenesis of gastroduodenal ulcer Arch franco belges de chir, 1930, 32 282 Abstracted in Internat. Abst. Surg, 1931, 52 22
- 32 WHIPPLE and associates
  - a HOOPER, G W, and WHIPPLE, G H Bile pigment and diet studies Am J Physiol, 1916, 40 332
  - b WISNER, F P, and WHIPPLE, G H. Variations in output and pigments during 24 hour periods Am J Physiol, 1922, 60 119
  - c SMITH, H P, GROTH, A H, and WHIPPLE, G H Bile salt metabolism. J Biol Chem, 1928, 80 659
- 33 WHITLOW Unpublished thesis Loyola University
- 34 YESKO, S A The effects of ligation of pancreatic ducts on gastric digestion. Am J Physiol, 1928, 86 483

dehydration while the cells in Walt's sections are often as shrunken and as different from the living cell as the raisin from the grape.

After I had used the method of Wilson for 5 years, my attention was called in 1929 to another supravital procedure which was devised by Terry. With increasing satisfaction and confidence I came more and more to rely upon this method and, for several years, I have used it exclusively for the tissue diagnosis during operation. The entirely new principle of Terry's sections is that instead of having to cut tissue very thin to get histological detail relatively thick sections are made with a biconcave razor and stained only on one side superficially with Terry's neutral polychrome methylene blue. The slice of moist tissue with the stained surface uppermost is examined with artificial transmitted light. The resulting microscopic picture is one of unexpected beauty and minute detail. Since only the uppermost cell layer is stained and the light is transmitted through the thick unstained part of the tissue slice, one has the impression of seeing a perfectly thin microtome section. The nuclei are stained a deep blue while connective tissue and muscle fibers are of a light rose color. High as well as low powers of the microscope may be easily employed. Few artefacts are encountered since freezing, fixing, boiling or dehydrating are completely avoided. Many of the cells are still alive and they are studied as nearly as possible as they are in the living body.

The microscopic picture remains for about 6 minutes, then the stain fades slowly. Sections may be restained or if more material is available, a new section may be cut.

The three following reasons persuaded me to accept Terry's razor sections as a routine method for tissue diagnosis during operation.

1. Terry's method avoids the greatest disadvantage of the frozen section, namely that the available tissue, when the biopsy specimen is very small is used up by the rapid method and the employment subsequently of other methods of diagnosis is impossible. The preliminary cutting of razor sections does not exclude the later use of paraffin embedding. Even thin razor sections are usually thick enough to be cut in paraffin or celloidin

TABLE I—COMPARISON OF MICROSCOPIC DIAGNOSES OBTAINED FROM TERRY'S SUPRAVITAL SECTIONS AND PARAFFIN SECTIONS

Organ	Complete agreement between Terry sections and paraffin sections	Agreement as to general diagnosis and frequency	Disagreement
Bladder	100		2
Endometrium	89		
Intestine	14		
Respiratory tract			
Thyroid gland			
Uterus	26		
Vagina and cervix	11		
Cervix uteri			8
Vagina			
Prostate	30		
Urinary system	30		
Bones and joints	30		
Lymphatic system	26		7
Mesothelium			
Total	1000	26	20
Percentage	100	2.6	2.0

Moreover the staining of sections with polychrome methylene blue does not prevent the subsequent staining of these with other stains for the methylene blue is extracted completely when the tissues are run through alcohol. The objections brought out against Terry's method that it does not furnish permanent sections are without weight because it should be the rule to follow the rapid method in every case with paraffin sections.

2. The second great advantage of Terry's method is the fact that it is so simple that the pathologist does not need a technician for the preparation of the section. The success of the method depends to a great deal upon this independence. Examination of the fresh surgical specimen by sight and touch, selection of the block, the cutting sensation with the razor, the avidity of the tissue for the stain, all these steps of preparing the slide often furnish immediate and essential information to the pathologist which a ready made microscopic section handed by the technician may never reveal.

3. In rapidity Terry's method is unsurpassed by any other histological procedure.

# HELLWIG TISSUE DIAGNOSIS DURING OPERATION

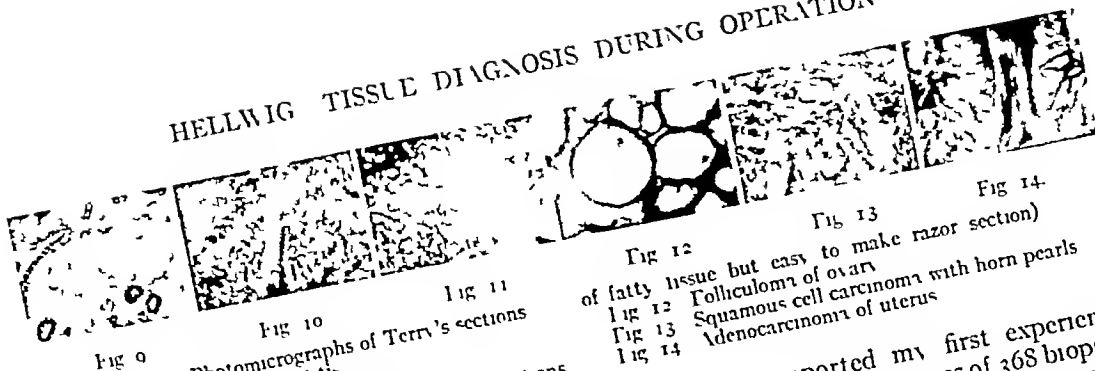


Fig 9 to 14 \* Photomicrographs of Terry's sections  
 Fig 9 Chronic cystic mastitis  
 Fig 10 Solid carcinoma of breast  
 Fig 11 Lipoma (it is impossible to make frozen sections of fatty tissue but easy to make razor section)  
 Fig 12 Folliculoma of ovary  
 Fig 13 Squamous cell carcinoma with horn pearls  
 Fig 14 Adenocarcinoma of uterus

In less than 1 minute the tissue is cut and stained. Therefore the study of several sections from different parts of the biopsy specimen is possible during the operation. Without causing delay for the surgeon it is easy not only to diagnose the local lesion but most accurately to determine the margin that should be given for a benign and for a malignant tumor and to ascertain whether glands near the local lesion which are exposed at the operation show metastases. Histological control of the whole tumor operation is made practicable by this ingenious method.

## RESULTS

Terry's method has proved itself reliable during the last 5 years not alone in the hands of the originator. The diagnoses made by Terry on razor sections of 2,000 tissues agreed in 96 per cent of the cases with those obtained by the pathologists of the Mayo Clinic using microtomes. Christeller, the German master of the microscopic art, was so impressed by Terry's method that he believed that it opened a new era in the field of biopsy. In 104 surgical specimens including 40 malignant neoplasms only three times was it impossible for him to make a correct diagnosis because of the unusual structure of the tumors which required special staining methods.

Figs 9-14 represent a stage in the development of a photographic technique which will bring about great improvement. Unsatisfactory as these photographs are at this time, they cannot give any impression of the beauty in color and the detail in structure presented by the razor sections.

The difficulty that the surface of the razor sections is relatively uneven is easily and almost subconsciously overcome by the microscopist by turning the micrometer screw while in photomicrography, a large absolutely flat field is indispensable. The Leica or Zeiss Contax Camera seems to be the only suitable apparatus for this special purpose because these cameras allow instantaneous photomicrography during observation through a second eyepiece.

The perfection of photographing these supravital preparations is imperative because only then it will be possible to have permanent records of these sections.

An excellent impression of the cell structure in supravital preparations is given by photomicrograph 7 which represents living cells of ovarian cancer stained with Terry's methylene blue.

In 1932 I reported my first experiences with Terry's sections in a series of 368 biopsies they allowed the same histological diagnoses as paraffin sections in 94 per cent. In 98 per cent both microscopic diagnoses were identical in regard to malignancy and benignancy.

The results obtained in my recent series of 1,030 biopsies including 303 malignant tumors, are recorded in Table I. Complete agreement between histological diagnoses obtained by razor and paraffin sections was found in 93.1 per cent while malignancy and benignancy was recognized correctly in 96.6 per cent of the razor sections.

Terry's statement that the easiest organ to diagnose is the breast is substantiated by my own experience. There was not a single disagreement between razor and paraffin sections in this field. Much more difficult to diagnose were small friable uterine scrapings and small papillomatous tumors of the bladder and the hardest tissues to diagnose were in my series

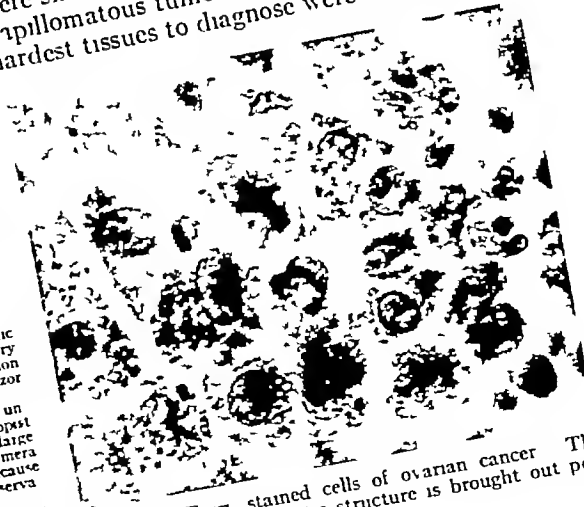


Fig 15 Terry stained cells of ovarian cancer. The nuclear and cytoplasmic structure is brought out perfectly by the supravital stain.

## TISSUE DIAGNOSIS DURING OPERATION

RELIABILITY OF TERRY'S SUPRAVITAL TECHNIQUE IN 1930 BIOPSIES

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THE committee on the treatment of malignant diseases of the American College of Surgeons endorses the rapid microscopic methods of tumor diagnosis, with the following advice: "In order that in patients with cancer the possibility of cure shall not be jeopardized, an exploratory operation should be conducted only under such conditions that the appropriate treatment, whether by surgery or by radiation, may be carried out immediately upon the establishment of the diagnosis by the pathologist by means of frozen sections."

It was not until Wilson in 1905 brought out his method of sectioning fresh tissue with the freezing microtome and staining it with poly chrome methylene blue that tissue diagnosis during operation became practicable. This method has been tried out in the Mayo Clinic during the last 25 years on more than 28,000 malignant tumors. Besides Wilson and MacCarty of the Mayo Clinic, Bloodgood deserves the greatest credit for introducing the microscopic diagnosis from rapid sections as a routine procedure. Bloodgood states that such a diagnosis is at least equal in accuracy to that made later from carefully prepared paraffin sections.

In appreciating the advantages of rapid sections, some authoritative pathologists have been as reserved as the surgeons have been enthusiastic. Having made more errors by the use of frozen sections in cases of breast cancer than by the gross examination, Ewing has not resorted to frozen sections in this field for many years. Reimann said that the very quick five minute fix, cut and stain diagnosis is looked on with suspicion by every good pathologist. According to Sternberg of Vienna, the rapid method is often unreliable, especially in borderline cases in which an exact microscopic diagnosis would be essential during operation. Also in Warthin's and Dietrich's opinion, immediate microscopic diag-

nosis during operation has a very limited field.

In the controversy regarding the usefulness of tissue diagnosis during operation, any general acceptance or condemnation cannot be made. In any method of diagnosis, the success depends upon familiarity with a given procedure and the experience of the observer. The morphological diagnosis of a tumor is occasionally very difficult whatever the method of preparation, and long study may be necessary before the final classification of the growth is possible. The pathologist must have the courage, in cases in which the rapid method does not permit a clearcut diagnosis, to admit his failure. Then no surgeon will be misled.

The present custom, less common in this country than in Europe, of burdening a young surgical assistant with the responsibility of diagnosing tissue sections, will never permit a high standard of microscopic diagnosis during operation. The surgical assistant is obviously more interested in the technical side of surgery and leaves the rotating service in the laboratory before he has acquired a wide experience which is indispensable, especially for the diagnosis of frozen sections.

## TECHNIQUE

The favorite rapid method used in German surgical clinics is that of Waltz. After the tissue is fixed in hot formalin for 1 minute, frozen sections are cut and stained with hematoxylin and eosin. For immediate diagnosis, during operation, the staining, dehydrating and clearing have to be hurried so that frequently very unsatisfactory pictures are obtained. In my experience, these poorly differentiated and distorted sections cannot compare with the beautifully stained preparations made by Wilson's supravital technique. The latter method enables one to see the intact cell, uninjured by boiling and

# HELLWIG TISSUE DIAGNOSIS DURING OPERATION

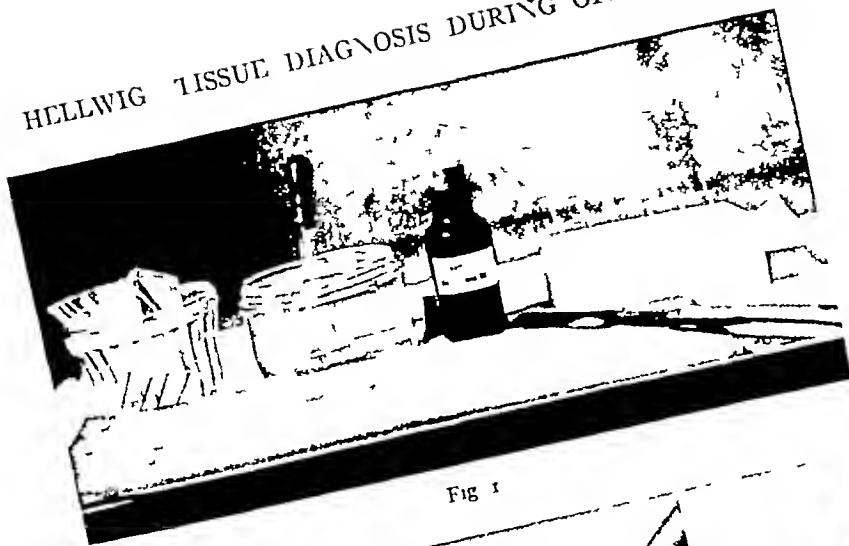


Fig 1



Fig 2

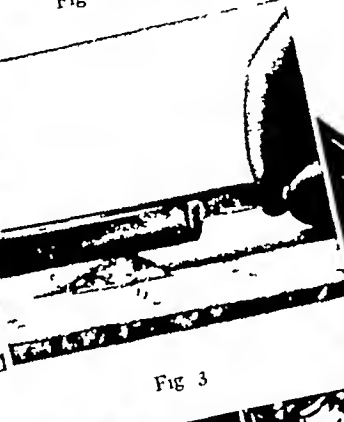


Fig 3



Fig 4



Fig 5



Fig 6

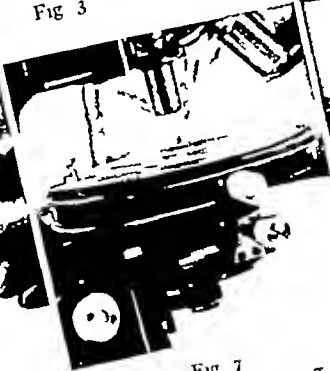


Fig 7



Fig 8

Fig 1 The equipment consists of a sharp biconcave razor a cork plate pins, a water tumbler a bottle of poly chrome methylene blue medicine dropper, glass slides and cover glasses  
 Fig 2 Pin selected piece of tissue to cork plate  
 Fig 3 Cut with razor a plane parallel slice from the wet tissue  
 Fig 4 Stain razor section superficially with methylene blue, for 1 to 3 seconds

Fig 5 Wash off carefully the excess of stain with tap water  
 Fig 6 Cover the stained surface firmly with a cover glass  
 Fig 7 Examine by transmitted light, using a 60 watt Mazda bulb Arc light is necessary to transilluminate bloody tissue  
 Fig 8 After examination preserve razor section in 10 per cent formalin for subsequent embedding in paraffin

non-carcinomatous lesions of the lymph nodes. In 4 instances Hodgkin's disease was erroneously diagnosed by razor sections, as tuberculosis. On the other hand carcinomatous metastases in lymph nodes were as easily recognized as the primary tumor.

In some tumors it was necessary to cut several sections before a diagnosis could be made. Very few razor sections were impossible of a diagnosis. In only 1.6 per cent of the biopsies was the surgeon informed that no definite diagnosis could be made by the rapid method. After removal of the tumor the wound was closed and the radical operation was not considered until a final histological diagnosis was obtained by means of paraffin sections. In these rare doubtful cases, it is obviously more in the interest of the patient to wait 24 hours for the preparation of paraffin sections than to proceed with a radical operation on suspicion only.

Malignancy was not recognized in 5 cancer cases from razor sections. Two of these cases, however, represented so called early cancer of the cervix and 1 was a small adenocarcinoma in a hyperplastic endometrium. In the 2 other instances the malignant changes were so minute that they were discovered only after studying many paraffin sections. These cases had metastatic cancer in lymph spaces of the neck and mesentery respectively.

Up to the present no false diagnosis of malignancy in a benign lesion has been given except in a case of cellular angioloma of the skin. From the razor section of the very bloody tissue I made the diagnosis of sarcoma. At this time I had not yet learned that hemorrhagic tissue can be easily transilluminated by using arc light in place of the 60

watt Mazda lamp which is satisfactory for most razor sections. Also in this case no harm resulted to the patient from the erroneous diagnosis, because the surgeon performed only a local excision of the tumor.

#### SUMMARY AND CONCLUSIONS

Terry's supravitral technique has been adopted as the most favored routine method of diagnosing tumor tissue during operation. Its reliability equals that of frozen sections.

In rapidity it is not surpassed by any other histological procedure, and it permits therefore, the microscopic control of a whole tumor operation without causing any delay to the surgeon.

It does not prevent subsequent employment of paraffin or celloidin sections, even if the biopsy specimens are of extremely small size.

It is noiseless and can be employed in the operating room without elaborate equipment.

#### BIBLIOGRAPHY

1. BLOOMBERG, J. C. Tumor diagnosis in the operating room. *South M J* 1928, 31.
2. C. KONTILLER, L. Erfahrungen mit der verbesserten histologisch diagnostischen Schnelkmethode nach Terry. *Klin. Wchnscheft* 1929, 7, 449.
3. HALLWIG, C. A. Das Probenpräparat. *Klin. Wchnscheft* 1929, 8, 52.
4. Ideas. Biopsy in tumors. *Arch. Path.* 1932, 3, 407.
5. TERRY, H. I. A new and rapid method of examining tumor macroscopically for malignancy. *J. Lab. & Clin. Med.* 1928, 13, 190.
6. Ideas. Improvement in technique and results made in examining macroscopically by the razor section method some malignant tumors. *J. Lab. & Clin. Med.* 1929, 14, 30.
7. WILSON, L. B. A method for the rapid preparation of fresh tissues for the microscope. *J. Am. M. Ass.* 1905, 41, 37.

## CLINICAL SURGERY

FROM THE SURGICAL SERVICE OF THE ROOSEVELT HOSPITAL

## A METHOD OF CLOSURE OF TEMPORARY EXTERNAL FECAL FISTULA

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FOR the past five years we have employed a method for the closure of temporary fecal fistulas which has been satisfactory. It has been used principally for the closure of temporary cecostomies and colostomies, however, it is equally applicable to small bowel fistulas. It is described for the reason that the operator for an occasional fecal stoma often wishes to know explicitly the steps of a relatively safe procedure and it is quite

infrequent that textbooks, monographs, or articles on this phase of intestinal surgery give a minute account. We claim no originality for the procedure, many others no doubt have followed the various steps in exactly the same manner. Usually

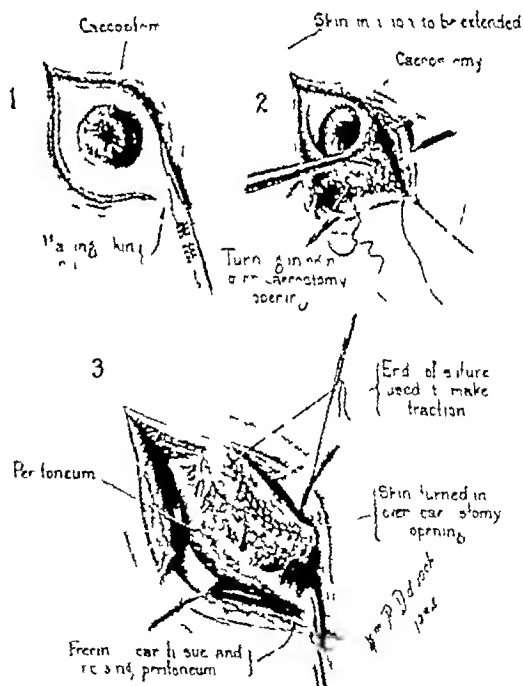
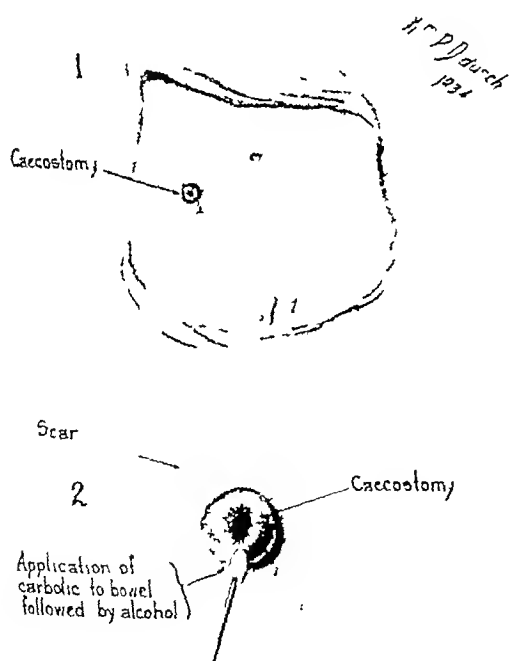


Fig 1 1 A pouting cecostomy stoma with the intermuscular incision completely healed above and below  
2 Phenol being applied in an attempt to sterilize the infected mucous membrane

Fig 2 1, An elliptical incision in the skin is made one inch away from the fistulous opening 2, The flaps of skin are carefully sutured over the opening with a continuous suture of medium sized silk, and the skin incision is then extended above and below 3 The ends of the continuous silk sutures are utilized for the purpose of traction, carefully but gradually pulling the closed in stoma out 2 inches above the level of the surrounding skin The muscular layer is separated and pushed away and when necessary the peritoneal cavity can at this stage be opened into



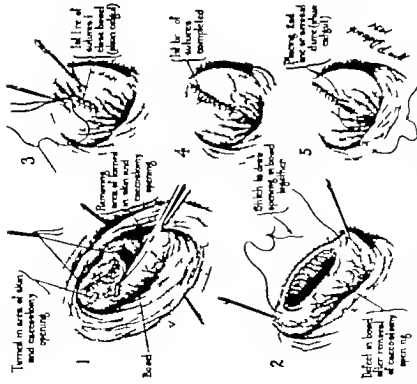


Fig. 3. Caecum is turned out, the bowel is then excised and healthy bowel is exposed ready for anastomosis. The opening into the lumen of the bowel is sutured in the center of the proposed line of closure. The defect is closed transversely to the long axis of bowel wall. A first layer of continuous suture is completed. A second layer anastomosis is made, continuous suture being used from beginning to end.

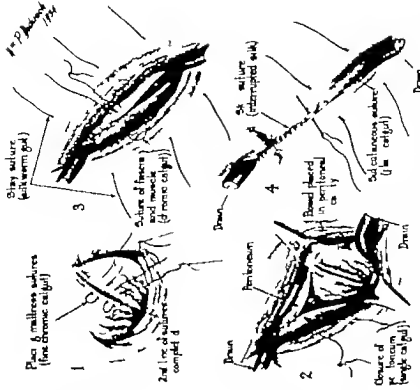


Fig. 4. Reinforced mattress sutures of fine chromic catgut are placed forming third tier of sutures. The closed bowel dropped back, inside the peritoneal cavity. Small drains are placed in either angle of the wound and the peritoneum closed. Stay sutures are placed and the muscles and fascia closed with figure of 8 fine chromic catgut sutures. A line plain catgut is used to bring together the subcutaneous tissue, skin to skin, stay sutures being used and end of drains protruding.



Fig. 2 Shows the various similar steps in the closure of a left sided colostomy temporary isthmus opening.

it is an intraperitoneal method. Yet we have on numerous occasions been able to close extraperitoneally, particularly if there is present a moderately thick layer of extraperitoneal fat for is traction is made on the temporarily closed stomach there is more give to the bowel loops themselves due to elasticity of the adherent extraperitoneal fat layer. We have had but moderate fear of peritonitis, for we, like others believe there exists a fair local immunity due to vaccination from the previous operative maneuver and the functioning stoma with its fecal flow. It is not an aseptic method, none that I know of are yet care is used to minimize unnecessary soiling.

Before an attempt is made to close a fecal isthmus it is obviously necessary to know that there is no obstruction present below in the intestinal tract. A practical pre operative measure, occasionally overlooked, is an enema or a colonic irrigation to clear away inspissated fecal matter one can well imagine impacted material in the rectum spelling failure to an otherwise satisfactory closure.

A thorough 3 day pre operative preparation will add considerably not only to the ease and neatness with which the procedure is carried out, but also to the comfort of the patient after operation. Furthermore, a supposed simple procedure

of closure of the colostomy may easily and frequently become a major surgical undertaking. For instance, a resection may be required and this would tax the vitality and resistance of a weak individual. The pre-operative preparation consists of a low residue diet for 3 days before operation, morphine sulphate  $\frac{1}{6}$  grain every 4 hours by the clock during the 26 hours just prior to operation, and 1,000 cubic centimeters 5 per cent glucose twice daily for 2 days before the day of operation. In patient with a rectal stoma often the skin surface about the opening is ventilated from the pouring forth of the content of the small intestine. We have found aluminum powder (the alkali breeding formula) a most

excellent protection against this painful and sometimes hazardous fecal irritant. A non-excoriated, healthy skin about the fistulous opening means much toward a rapidly and completely healed wound.

I have used this procedure twenty-eight times and in no instance has there been the necessity of a second operation. In three there occurred a "pitting out" of stoma and a small amount of fecal matter for several days followed by spontaneous closure.

The accompanying illustrations with the descriptive notes below seem sufficiently clear to obviate the necessity of an further explanation of the operative procedure.



TABLE I.—RACE OR NATIONALITY OF 210 PATIENTS IN RELATION TO MORTALITY

Race	Patients	Deaths	Mortality* per cent
American negroes	38	—	99
Irish	34	9	26.4
Italians	13	5	5
West Indians	24	—	4
Americans	0	3	57
Jews	7	—	6
German	5	3	20
Poles	5	4	—
Greeks	4	—	—
Spaniards	3	—	—
Hungarians	3	—	—
English	—	—	—
Scottish	—	—	—
Canadians	—	—	—
Lithuanian, Russian, Slovak, Finnish, Bohemian, Japanese, Bulgarian, Scandinavian, French, each	9	6	—
Total	—	—	59

\*Mortality not computed for groups under ten in number

important, they are often slender props to lean upon. The clinical picture of spina atrophy limp and deformity applies equally to suppurative arthritis in many instances so the diagnosis may well be uncertain until tissue or exudate is examined.

In 10 of the 224 different joints, the evidence was conclusive after tissue examination or guinea pig inoculation. In 110 cases the spine was involved and since in these cases it is impossible to get pathological corroboration unless an abscess can be aspirated or another joint is involved which may be explored, it will be appreciated that a very high percentage of the available joints were proved cases (see Table IV). If the spine

TABLE II.—RELATIVE FREQUENCY OF INVOLVEMENT OF THE VARIOUS JOINTS IN THIS SERIES

	No.	Per cent
Weight bearing joints		
Spines	—	49.3
Knees	44	9.7
Hips	5	—
Sacro iliac joints	6	7
Tarsal joints	3	5.8
Ankle joints	4	8
Synphysis pubis	—	4
Total lower extremity or spine	3	95.3
Non weight bearing joints		
Shoulders	—	8
Elbow	5	3
Wrist or carpal joints	4	6
Total upper extremity	—	4.7

cases were subtracted it will be seen that 87 of 113 available joints, or 76.5 per cent, were proved positive. In 14 spine cases it was possible to recover tubercle bacilli or tissue to add to the certainty of diagnosis.

*Principles of treatment.* Our treatment has been carried out with the idea that each patient has systemic tuberculosis. We have often kept patients in bed for several months before operation and for 8 months to a year after operation. They have had as good food as possible and during the summer months all the sunlight that our climate affords. All of our children get cod liver oil. The operative treatment aims to eliminate the surgical focus by putting the joint or joints involved at complete rest, and the most effective means of accomplishing this is by operative fusion. If an extremity joint is overwhelmingly involved and any attempt to save it endangers the patient's life, amputation is resorted to.

*The patient in relation to his tuberculosis.* In considering these patients from the standpoint of their systemic tuberculosis, we have divided them into four main groups as follows:

A. Patients with pulmonary tuberculosis and positive sputum.

B. Patients with pulmonary tuberculosis and negative sputum with metastatic spread to other organs.

C. Patients with pulmonary tuberculosis and negative sputum, with no metastatic spread to other organs.

D. Patients with evidence of no pulmonary tuberculosis.

The total number in each group and the mortality is given in Table V. It will be seen that among the 93 patients in groups A and B there occurred 48 of the 59 deaths while the remaining 7 patients had only 1 death among them.

The group with the positive sputum and cavities in the lungs should, in all probability be absolutely voided as operative choice. Unfortunately the second group with inactive pulmonary disease but with metastatic spread to other organs frequently can not be recognized prior to operation and will always furnish a large part of the mortality in any series of cases of joint tuberculosis. Here are the cases of tuberculosis of the genito-urinary tract, meninges, and peritoneum. We have seen these metastases develop too often in patients awaiting operation to believe that the operative procedure plays any part in the spread.

*Follow-up in relation.* The follow up in group of patients who are notorious drifters is extremely difficult. In spite of this, our average

TABLE III—OPERATIONS PERFORMED ON THESE 210 PATIENTS

	Operations	Total operations
I Spines		
1 Spine fusion	109	
2 Spine fusion and laminectomy	9	
3 Exploration of spine for pseudarthrosis	9	
4 Laminectomy on fused spine (for paraplegia)	2	129
II Knee joints		
1 Knee fusion	41	
2 Amputation	5	
3 Repair pseudarthrosis	4	
4 Biopsy	2	
5 Osteotomy of fusion for flexion	1	53
III Hip joints		
1 Fusion	25	
2 Repair pseudarthrosis	2	
3 Repair second pseudarthrosis	1	
4 Biopsy	1	
5 Osteotomy for deformity	1	30
IV Sacro-iliac joint		
1 Fusion	17	17
V Tarsal joints		
1 Fusion	9	
2 Amputation	4	13
VI Ankle joint		
1 Fusion	3	
2 Amputation	1	4
VII Symphysis pubis		
1 Fusion	1	1
VIII Upper extremity joints		
1 Fusion	11	
2 Repair pseudarthrosis	2	
3 Amputation	1	14
Total operations		261

TABLE IV—INCIDENCE OF POSITIVE DIAGNOSIS

The diagnosis was proved by tissue examination or guinea pig inoculation in various joints as follows

	Total	Number proved positive
Joint		
Spines	110	14
Knees	44	35
Hips	25	18
Sacro-iliac	16	13
Tarsal	13	7
Ankle	4	4
Symphysis pubis	1	0
Upper extremity	11	10
	224	101

tion I have rated these patients in three groups as far as results are concerned

a *Excellent*—those patients with solidly fused joints, with no active pulmonary disease, who can and have left the hospital to resume a relatively normal life

b *Uncertain*—those patients with solidly fused joints in most instances but with active pulmonary disease or amyloid disease from prolonged suppuration. Many of these patients have or have had positive sputum. Some are still in the hospital. Many have left the hospital but we have no feeling of security for their future

c *Died*—this is the only group that we can be absolutely certain about

#### TUBERCULOSIS OF THE SPINE

In this series 113 patients had tuberculosis of the spine and 110 of these were treated surgically. In 85, the spine was the sole focus while in 25, there was an additional joint or joints involved. The number of male patients was 64, of females, 46. Five patients were under 5 years of age, the oldest was 62, average age at onset was about 23 years (see Table VI).

*Duration of symptoms* The average duration of symptoms was 3 years and 2 months. The longest period was in a patient in whom the condition had persisted for 32 years prior to operation. In 7 the condition had persisted over 10 years. In 17 patients the disease had been present less than a year.

*Diagnosis* The diagnosis was made by physical examination and roentgenogram. Backache or pain was generally complained of and there was almost invariably spasm, tenderness, and deformity. The roentgenogram showed a thin intervertebral space progressing to actual destruction of the vertebral body above and below with abscess formation. In 14 cases it was possible

final follow-up examination has been 3 years. We have not relied on correspondence but have seen and examined each patient.

*End-results* Any attempt to gauge accurately the end-results in cases of joint tuberculosis is fraught with great difficulty. One has only to see non-operative patients who have had their disease light up after 30 years of quiescence or to have sent home patients with fused knees and hips in excellent condition and then several years later to see them die of tuberculous meningitis, to realize that we are dealing with an insidious disease of extreme chronicity. Each of these patients is in constant danger. Our operative treatment at best leaves them with stiffened joints which are better by far than the active disease, but there can be no restitution of func-

TABLE V—MORTALITY IN RELATION TO EXTENT OF SYSTEMIC TUBERCULOSIS INFECTION

	A	B	C	D
	Patients with pulmonary tuberculosis and positive sputum	Patients with pulmonary tuberculosis and negative sputum, with metastatic spread to other organs	Patients with pulmonary tuberculosis and negative sputum, with no demonstrable spread to other organs	Patients with evidence of no pulmonary tuberculosis
Entire group				
Patients	33	36	60	37
Deaths	34	24	7	
Mortality per cent		66	11	
Tuberculosis of spine				
Patients		37		24
Deaths		23	1	
Mortality per cent		62	25	
Tuberculosis of knee joint				
Patients		5		20
Deaths				
Mortality per cent		0		
Tuberculosis of hip joint				
Patients				6
Deaths				
Mortality per cent				100
Tuberculosis of sacro-iliac joint				
Patients		7		
Deaths				
Mortality per cent		60		
Tuberculosis of thoracic cavity				
Patients		3		
Deaths				
Mortality per cent		60		
Tuberculosis of upper extremity joints				
Patients				
Deaths				
Mortality per cent		75		
Multiple foci group				
Patients				
Deaths				
Mortality per cent		75		

to recover tubercle bacilli or tuberculous tissue from abscesses or additional joint foci, to add to the certainty of the diagnosis.

*Areas of spine involved.* These 60 spines, including additional spine foci in some instances were distributed as follows: 3 cervical, 4 cervico-dorsal, 60 dorsal, 12 dorsolumbar, 30 lumbar, 5 lumbosacral.

An examination of the individual vertebrae involved shows the great bulk of the lesions in the lower dorsal vertebrae with the cervical spine infrequently involved, while the lumbar spine is quite often the site of the disease. In this series the apex of maximum involvement extends from the seventh dorsal to the twelfth dorsal (see Chart 1).

*Paraplegia.* Among the more important complications of tuberculosis of the spine is paraplegia. This was first noted and described clinically by Sir Percival Pott in a paper titled "Remarks on that kind of palsy of the lower limbs which is frequently found to accompany curvature of the spine and is supposed to be caused by it." London 1779.

The spinal cord pressure is caused by an abscess and not by bony deformity. It is associated chiefly with disease of the dorsal spine. In this series 33 patients, or 29 per cent of the total, showed these symptoms. The vertebrae involved extended from the first dorsal to the first lumbar with the maximum involvement at seventh, eighth, and ninth dorsals (Chart 2). Paraplegia may occur at any age (see Table VI).

The symptoms vary from mild spinal cord pressure with resulting stiffness, weakness, and awkward gait. Increased activity of the reflexes, and impaired sensation of the lower extremities to complete spastic paralysis with anesthesia and loss of control of the anal or urinary sphincter or both. Bed sores develop only in the most severe cases and then usually as terminal manifestations.

Eight of these patients presented evidence of mild or incomplete pressure, while the 25 remaining had complete paraplegia. The mild cases all cleared up spontaneously and, with one exception, occurred before any operative procedure had been instituted. This single exception was in a patient who 5 years after spine fusion showed weakness, mild spasticity and sensory disturbance, which cleared up after a few months' rest in bed.

The 25 patients with evidence of serious spinal cord pressure presented a more complicated problem. Ten of them developed symptoms before operation and 5 afterward. In this group the symptoms cleared up in 13 patients, and in 12 there was no improvement; these latter all died of the disease at an average of 9 months after operation, a 48 per cent mortality. Those patients who failed to recover were for the most part in the groups in which failure to survive is frequent, e. those with positive sputum and those with negative sputum but metastatic spread to other organs.

Laminectomy was performed on 11 patients, of whom 6 recovered and 5 did not. This operation was at times done in conjunction with a fusion and at times subsequently. In each instance a definite block in pulsation of the spinal cord was noted. Tuberculous granulation tissue was often found over the dura, which was not opened.

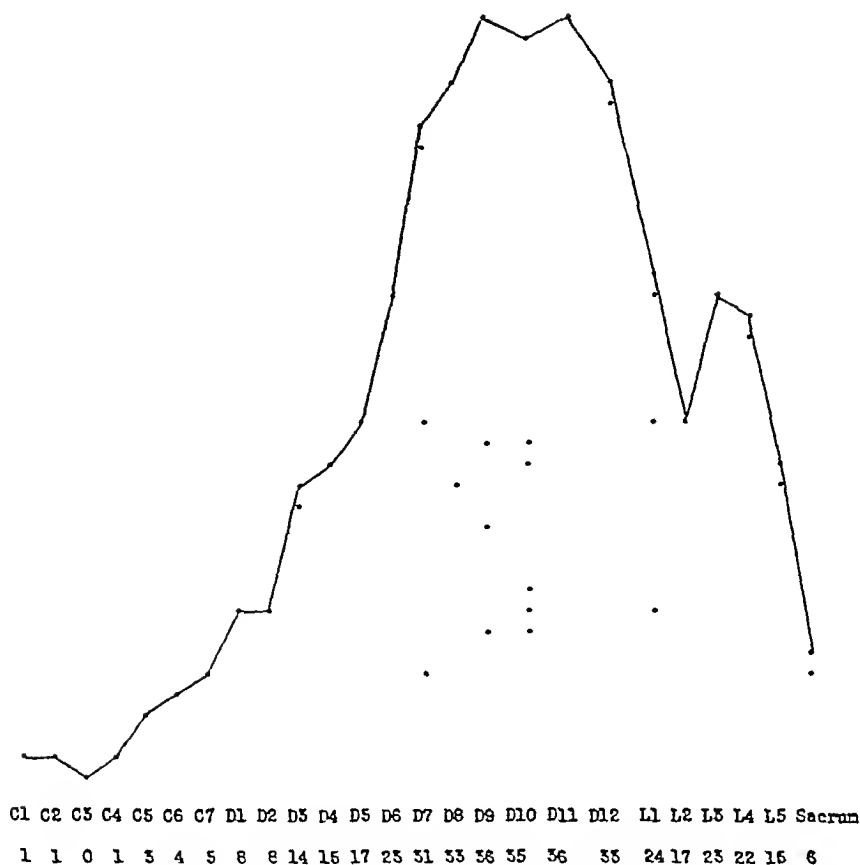


Chart 1. Vertebrae involved in this series of 110 patients

There were several instances in which, following the operative release of pressure, the symptoms cleared up with dramatic speed. One child of 9, whose paraplegia had been complete for 4 months, had recovered almost entirely 2 weeks after operation.

**Abscess.** Either paravertebral or psoas abscess was noted in 75 of these 110 operative spine cases. Many of these were repeatedly aspirated successfully, thus preventing sinus formation. In healing the abscesses tended to calcify. Of the 75 patients with abscesses, 29 died, a mortality of 38.6 per cent.

**Sinuses.** Sinuses increase the gravity of the problem greatly. Amyloidosis after prolonged suppuration is too well known to require comment. Twenty-four patients had sinuses and 13 or 54 per cent died.

**Treatment.** In these 110 operative spines the surgical treatment has been spine fusion of the

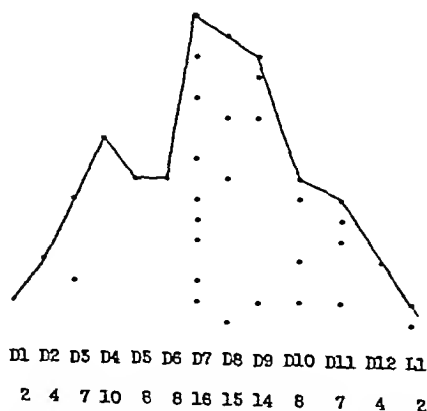


Chart 2. Vertebrae involved in those 33 patients developing paraplegia.



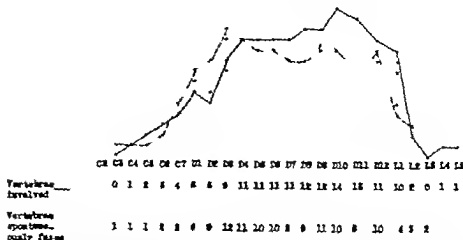


Chart 1. Spontaneous fusion, showing in 5 patients the relation between vertebrae involved in the disease and those spontaneously fused. The broken line designates the vertebrae spontaneously fused while the continuous line designates those involved by the disease. In some instances, such as at third cervical and from seventh dorsal to third dorsal, vertebrae spontaneously fused existed in number those involved by the disease, which illustrates the mechanical nature of this attempted repair.

Hibbs type extending from a sound vertebra above and below. In a few cases the fusion has included only 1 sound vertebra above and below.

**Spontaneous fusion.** At operation spontaneous fusion was found in 25 patients. In 4 others there was noted a partial or incomplete fusion. The age of these patients with spontaneous fusion was distinctly young, 64 per cent of them being under 20 years of age (see Table VI). The average duration of symptoms was almost 6 years, which is twice that for the entire series of 110 patients with tuberculosis of the spine.

Nineteen of the 25 had a long rather sharp kyphos involving an average of 8 vertebrae of which the average number spontaneously fused was 6. The 6 remaining had only a moderate kyphos, with an average of only 3 vertebrae spontaneously fused.

The longest spontaneous fusion was 12 vertebrae, and there was one instance of 11 vertebrae, and another of 10 vertebrae. Two patients had 2 separate areas of spontaneous fusion. In most instances, vertebrae above and below were operationally added to those spontaneously fused as the area was inadequate. If there were 2 separate areas of spontaneous fusion these were connected and additional vertebrae were added above and below. In one patient with 1 vertebra spontaneously fused, no vertebrae were added, as the fusion was considered mechanically adequate.

Chart 3 shows graphically the relation between those vertebrae involved in the disease and those spontaneously fused. It is interesting to note that, in some instances, the vertebrae spontaneously fused were outside the diseased area but were mechanically in the kyphos. This heroic effort of nature to remedy a bad mechanical situation in the spine that has arisen from destruction of vertebral bodies is, of course, the inspiration for our surgical treatment of this disease. Unfortunately nature works slowly and with tremendous deformity. These patients who showed this reparative phenomenon of spontaneous fusion had had the disease for many years with severe destruction of vertebral bodies and great deformity for the most part. They are a group with greater resistance to the disease than most. Of the 25 but 5 died, 20 per cent mortality. These deaths were due to metastatic spread to other organs in 2 instances, to amyloid disease in 1 and the remaining 2 fatalities were cardiac deaths.

**Failure of fusion or pseudo-arthrosis.** We have had no braces available at Sea View Hospital and have not used plaster-of-paris jackets, so our patients have had no postoperative immobilization, except to lie flat on a fracture board. The question of solid bony fusion is of the utmost importance so we have carefully examined each patient and have had postoperative roentgenograms

TABLE VI—AGE INCIDENCE IN VARIOUS FORMS OF JOINT TUBERCULOSIS

Years	Patients with tuberculosis of spine			Patients with tuberculosis of knee joint	Patients with tuberculosis of hip joint	Patients with tuberculosis of sacro-iliac joint	Patients with tuberculosis of tarsal joints	Patients with tuberculosis of upper extremity joints	Patients with multiple joint foci
	Entire group	With paraplegia	With spontaneous fusion of spine						
1-10	4	5	6	4	9	0	1	1	8
11-20	20	4	10	12	6	5	3	4	15
21-30	26	8	4	15	7	7	3	3	11
31-40	17	6	2	3	2	3	2	1	7
41-50	14	7	2	10	1	1	3	1	1
51-60	8	2	1	0	0	0	1	1	1
Over 60	1	1	0	0	0	0	0	0	0
Total	110	33	25	44	25	16	13	11	43

made at intervals. Though the fusion may seem solid clinically, it is very rare, except in children, that the roentgenograms show a satisfactorily calcified bony mass under 6 months. With the increasing kyphos, persisting pain and spasm, failure of fusion may be suspected and the roentgenogram may show it.

*End-results of tuberculosis of spine.* From the standpoint of operative technique, we have had occasion to doubt that fusion was solid in 15 cases. In 5 of these the operation was done at other hospitals, of these, 3 were of the Hibbs type and 2 were bone grafts of the Albee type. At operation one Hibbs fusion was found solid with adequate bone and the 2 others were repaired. The tibial bone grafts were too short, had fractured at the center, and were partly absorbed. These also were repaired. Of the 10 remaining cases which were originally operated upon at Sea View Hospital, 4 when explored were found to have solid, massive, bony fusion. Three of these were in children whose kyphos had definitely and markedly increased, apparently due to massive vertebral destruction and the final deformity was assumed after the diseased bodies settled into contact.

Of the 6 remaining suspected of failure of fusion, 1 patient would not permit a second operation. The 5 others were proved to have failure of fusion at the second operation and were repaired. These failures, except 1 in the dorsal spine, were at the dorsolumbar junction or upper lumbar spine, an area of great mobility and strain in which we might anticipate a certain number of failures. The incidence of only 5 proved cases of failure of fusion in 110, or 4.5 per cent, speaks highly for the effectiveness of the operative procedure. We have had ample opportunity to observe the effective massive fusions that occur in most instances. At postoperative laminectomy,

we have found this mass of bone as thick as five-eighths of an inch covering the laminae and forming an entirely adequate brace.

The end-result rating of these 110 patients will be seen in Table VII.

In analyzing cases of tuberculosis of the spine in relation to their systemic tuberculosis, we find practically 80 per cent of the mortality lies among those patients with positive sputum or metastatic spread to other organs (see Table V).

Of the 32 who died with tuberculosis of the spine, 29 had abscesses and 13 had sinuses. Deaths in the more favorable groups were due to amyloid disease and in one or two instances to cardiac disease.

In analyzing these deaths in tuberculosis of the spine in relation to age, we find that the mortality in the first decade is low and that it reaches its maximum in the third decade (see Table IX).

An analysis of the deaths in relation to the area of the spine involved shows that there is a pretty even distribution with the lumbar spine showing a slightly higher mortality rate (see Table VIII).

#### TUBERCULOSIS OF THE KNEE JOINT

In our experience tuberculosis of the knee joint is the most favorable site for surgical treatment. The joint is easily explored for diagnostic purposes and is not difficult to fuse.

In this series, there were 44 cases of tuberculosis of the knee joint. In 36 of these the knee joint was the only joint involved while the remaining had other joints affected. Male patients had the disease three times as frequently as female, there being 33 of the former and 11 of the latter.

The condition is almost invariably treated as rheumatism for months or years before it is

TABLE VII.—END-RESULTS OF TUBERCULOSIS OF THE JOINTS

Rating	No. cases	Per cent	Average time after operation
<b>Spine—30 cases</b>			
Excellent	20	66	7 yrs 6 mos
Uncertain	7	23	7 yrs 6 mos
Dead	3	10	
<b>Knee—44 cases</b>			
Excellent	27	61	7 yrs 6 mos
Uncertain	1	2	7 yrs 6 mos
Dead	16	36	
<b>Hip—25 cases</b>			
Excellent	6	24	7 yrs
(a) with solid bony fusion			
(b) with 2-3 degrees ankylosis			
Uncertain	—	—	—
(a) with solid bony fusion			
(b) not fused			
Dead	1	4	7 yrs
(a) with solid bony fusion			
(b) not fused			
<b>Sacro-iliac joints—16 cases</b>			
Excellent	17/16	100	7 yrs 2 mos
Uncertain	1/16	6	7 yrs 6 mos
Dead	1/16	6	
<b>Thoral joints—43 cases</b>			
Excellent	70	161	7 yrs 6 mos
Uncertain	43	100	6 mos
Dead	—	—	—
<b>Ankle joints—4 cases</b>			
Excellent	1	25	7 yrs
Uncertain	—	—	—
<b>Upper extremity joints—5 cases</b>			
Excellent—neck solid fusion			
Shoulder			
Elbow			
Wrist solid fusion—elbow			
<b>Thoracic—without fusion—elbow</b>	13	100	7 yrs 6 mos
Dead—carpus	13	100	
<b>Multiple joint—43 cases</b>			
Excellent	30	69	7 yrs 6 mos
Uncertain	14	31	7 yrs 6 mos
Dead	—	—	—
<b>30 patients of the multiple joint series who had second joint operated upon</b>			
Excellent	70	Over 1 yr	
Uncertain	30	7 yrs	
Dead	30	13 yrs	depr—

46/75  
 12 months (except ankylosis who died within 24 hours, and 43  
 46/75  
 12 months (except ankylosis who died within 24 hours after second operation)  
 (the lower after operation of ankylosis (two deaths—also noted under  
 sacro-iliac cases)

recognized. The average duration of symptoms before operation was 4 years. Two patients had had their disease for 10 years and 1 for 4 years.

Age. The age incidence of this group of 44 patients is fairly evenly distributed in the first 5 decades (see Table VI). Average age at onset was 3 years.

Diagnosis. The diagnosis was made by physical examination, roentgenographic study and a

study of excised tissue. The diagnosis was proved positive by tissue examination in 35 of 44 patients. Six cases were explored, found negative for tuberculosis, and not fused.

Sinuses. Sinuses were present in 31 of the 44 patients with knee joint tuberculosis.

Operative and postoperative treatment. The operation employed was a fusion of the knee joint, the patella being used as a peg fitted into a prepared mortice in the femur and tibia as described by Habbe. After operation, a plaster-of-paris spica was applied for 6 to 8 weeks, followed by a long leg circular plaster until fusion became solid. The length of time required to accomplish bony fusion varied from 4 months to a year or more. The progress of fusion was checked by clinical examination and roentgenogram. Weight bearing with a long circular plaster splint was permitted after 6 months, if the patient's general condition warranted it.

We have had occasion to observe several children whose knee joints had been resected at other hospitals and as they reached full growth the leg with the resected knee was between 6 and 7 inches shorter than the sound leg with the disease still active. I should like again to condemn utterly this procedure in children.

End-results. A knee fusion was done in 41 cases and an amputation in 3 cases in which fungating sinuses made any attempt to save the extremity impossible. Fusion became solid in 34 of 35 surviving patients on whom it was attempted, though 4 of them required a second operation. Fusion was also solid in patients who died of their systemic disease 2 or 3 years after operation. This testifies to the efficacy of the operative procedure. The end-results are shown in Table VII. Seven patients who failed to attain fusion of the knee joint were all fatal cases, overwhelmed by their tuberculosis and profuse suppuration. Of 31 patients with sinuses, 18 survived. We have had the discouraging experience of sending a patient home in excellent condition with a solidly fused knee and then watched him die 2 1/2 years later of tuberculosis of the meninges. Morbidity was highest in the third decade (see Table IV).

Fusion in children. There were 3 young patients 6, 3, and 3 years of age respectively. Each had a large fungating synovial type of disease. Fusion was obtained in each of these patients though required a second operation to make solid bony contact. The diseased leg in these youngsters has kept up in growth with the sound leg. Fusion on these small knee joints is technically difficult but worth attempting when we consider that 4 of our patients with this disease

TABLE VIII—MORTALITY IN PATIENTS WITH TUBERCULOSIS OF SPINE IN RELATION TO THE AREA OF THE SPINE INVOLVED

	Number of patients	Died	Mortality per cent
Cervical	3	1	33
Cervicobrachial	3	1	5
Dorsal	60	16	26.7
Dorsolumbar	12	1	8.3
Lumbar	10	10	100
Lumbosacral	5	1	20

entered the hospital as infants and spent 14, 8, 7 and 6 years respectively, an average of about 9 years each, while various forms of immobilization were tried. At the end of this period each of these patients had active knee joint tuberculosis. In each instance a fusion was done and the patient was discharged from the hospital within a year after operation.

Mortality in relation to systemic tuberculosis is shown in Table V. Cases with positive sputum or metastatic spread to other organs furnished 88 per cent of the total mortality. The one death in a favorable group was from amyloid disease.

#### TUBERCULOSIS OF THE HIP JOINT

There were 25 patients in this series with tuberculosis of the hip joint, a majority of them males. The right hip was involved 15 times and the left 10 times.

The age of this group was relatively young, 88 per cent of them being under 30 years. The youngest was 3 years and the oldest 41 years (see Table VI). The average age at onset was 13 years.

**Duration of the disease.** The average duration of the disease prior to operation was about 4 years. Three cases had persisted 10, 15 and 10 years, respectively.

**Diagnosis.** The diagnosis was made by clinical examination, showing spasm, limited motion, flexion and adduction deformity, limp, etc., and by roentgenographic evidence of a destructive arthritis involving the head of the femur and at times the acetabulum. In most instances the disease had advanced to the stage of bone destruction, but in a few instances it was limited to the synovia. In one instance, a preliminary biopsy was done.

In 18 of the 25 fusions, the tissue removed at operation proved the diagnosis to be tuberculosis. Due to massive destruction, fusion of the unproved joints was completed.

**Abscess and sinuses.** Abscess was present in 21 of the 25 patients. Sinuses were present in 12 patients prior to operation and developed in 3 others after operation. These facts, I believe,

support the contention that the group was an unfavorable one on which to get brilliant surgical results.

**Treatment.** In our experience fusion of the hip joint in tuberculosis is not easily accomplished. In case there is massive destruction of the head and neck of the femur due to long standing disease, giving an unstable joint, it is doubtful if fusion can be accomplished by any of the methods that have been described.

An operative fusion of the hip was attempted on each of these 25 patients. The Hibbs type—the great trochanter and a piece of the shaft of the femur being rotated on the muscle attachment and driven into the ilium just above the acetabulum—was employed in 10 cases. In the 15 remaining cases a large mass of ilium was used to form a bridge from a deep socket in the femur to the denuded ilium. This type of fusion was first done in 1927. With the Hibbs method we had only 3 successful fusions in 10 attempts, whereas by the second method there were 10 successful fusions in 15 attempts.

We have immobilized the hip by a double plaster-of-paris spica for 4 to 6 months and then applied a single spica for an additional period until we felt that fusion was solid by clinical and roentgenographic examination or else until we abandoned hope of fusion.

**End results.** These are summarized in Table VII.

Subtracting the 8 unfused hips that terminated fatally, the operation was technically successful in 13 of 17 cases, or 76 per cent. Two cases required secondary operations. The failure to obtain a higher percentage of operative success was almost certainly due to the presence of sinuses in 50 per cent of the cases.

**Analysis of mortality of 25 patients with hip joint tuberculosis.** There were 3 patients who died within 36 hours after the operation of whom 2 were adults with cardiac disease. One patient discharged from the hospital as an excellent result with a solidly fused hip, died of tuberculosis of the meninges  $3\frac{1}{2}$  years after operation. Sixty-six per cent of the total mortality occurred in patients with positive sputum or metastatic spread to other organs. The 3 deaths in the more favorable groups were due to cardiac disease twice and to amyloid disease once (see Table V).

**Age.** The age in relation to mortality shows the third decade leading again (see Table IX).

#### TUBERCULOSIS OF THE SACRO-ILIAC JOINT

In this series there were 16 patients with tuberculosis of the sacro-iliac joint, with the disease

TABLE IX.—ANALYSIS OF DEATHS IN RELATION TO AGE IN THE 3 LARGER GROUPS

Decade	Tuberculosis of spine			Tuberculosis of knee joint			Tuberculosis of hip joint		
	Number of patients	Dead	Mortality per cent	Number of patients	Dead	Mortality per cent	Number of patients	Dead	Mortality per cent
1-10	14		16						17 1/2
11-20	20	6	30			14 6	6		41 6
21-30	16		46	5	6	48			87
31-40	7	6	85 7			22 1/2			90
41-50	14		28	20					
51-60	6	3	50						
Over 60									
Total	70	15		25	6		1	1	

in the right joint in 12 instances and in the left in 5. Seven were males and 9 females. Only 6 of these patients had tuberculosis of the sacro-iliac joint as the sole joint manifestation while 10 of them had other joints involved. Of these, 1 had both sacro-iliac joints invaded.

**Age.** No patient was under 11 years of age while 75 per cent were between the ages of 21 and 30 years (see Table VI). The average age at onset of disease was 24 years.

**Diagnosis.** The diagnosis was made by physical examination and roentgenogram. The chief complaint was low backache and stiffness. On examination they showed marked muscle spasm, pain on straight leg raising and extreme rotation of the hip, the pain being referred to the joint involved. The roentgenogram showed a destructive arthritis of the joint with marked atrophy of the adjacent ilium and sacrum, clear cut in some cases, indefinite in others.

The diagnosis was proved positive by excised tissue in 13 of the 16 patients.

Abscess was present in 33 per cent of the patients and sinuses formed in 37 per cent.

**Surgical treatment.** An operative fusion was performed on each of these 16 patients, extra-articular in 13 and articular in 4 instances. The extra-articular fusion was performed by exposing the ilium and sacrum subperiosteally above and below the posterior superior iliac spine and then denuding the non-articular area between the ilium and the sacrum. A block of bone from the iliac crest was wedged into a prepared bed between the ilium and the sacrum and bone chips were packed around the entire denuded area. This method was used from 1916 to 1930. It is not as satisfactory, I believe, as the articular type of operation of Smith-Petersen which is used at present.

**End-results.** These are summarized in Table VII.

The presence of fusion in the sacro-iliac joint is difficult to determine with certainty. In many instances, either clinically or by roentgenographic examination. However we believe that all our surviving patients have solid fusion.

**Analysis of the mortality of 16 patients with sacro-iliac joint tuberculosis.** Our experience in this relatively small series has made us feel that sacro-iliac joint tuberculosis is a very serious manifestation with a mortality which is high for joint tuberculosis.

In this series, 75 per cent of the patients with tuberculosis of the sacro-iliac joint were in the groups with active pulmonary disease, positive sputum, cavities in the lungs, etc., or if they had a negative sputum their disease manifested itself by metastatic spread to other organs. These patients furnished 60 per cent of the mortality (see Table V).

#### TUBERCULOSIS OF THE TARSAL JOINTS

There were 13 cases of tarsal joint tuberculosis in this series, in one of which the ankle joint was also involved. The diseased joints were distributed as follows: 5 subastragalar joints, 4 tarsometatarsal joints, 3 entire tarsus, 1 calcaneus.

The disease was distributed almost equally between the sexes with 7 males and 6 females. The right foot was involved 4 times, and the left 9 times.

**Age.** The distribution by age showed a wide spread from the first to the sixth decade (see Table VI). The average age at onset was 26 years.

**Duration of the disease** was long, the average being 3 years and 9 months before operation.

**Diagnosis.** The diagnosis was made by physical examination, swelling, tenderness, marked muscle spasm. The roentgenogram showed a destructive arthritis with extensive atrophy. Sinuses were

TABLE \ —CASES WITH MULTIPLE JOINT FOCI WITH SUMMARY OF THE JOINTS INVOLVED

Joint or focus	Operation performed at Sea View	Elsewhere	No operation
Spine	25	1	3
Hip	5		5
Knee	5		2
Sacro-iliac	9		
Both sacro-iliac	1		
Second spine focus	3		2
Shoulder	1		2*
Elbow	2	1	7
Wrist	3		5
Tarsus	2		4
Ankle			1
Dactylitis	2		3
Tendon sheath	2		
Ribs	1		3
Scapula			1
Maxilla			1
Total	64	2	37

\*Shoulders in one patient.

present in 9 out of 13 patients. The diagnosis was proved by examination of the tissue removed in 7 of the 13 cases.

One patient in addition to tuberculosis of the tarsus had most extensive gout. His entire fore-foot showed masses of uric acid crystals all through the metatarsal bones. This patient died of advanced pulmonary tuberculosis.

*Surgical treatment.* Amputation through the upper third of the leg was resorted to in 4 cases with extensive widespread disease with abscess and sinuses. These patients all convalesced uneventfully. Fusion of tarsal joints was done by simple removal of the articular cartilage. Post-operative fixation by plaster boot was maintained for 4 to 6 months.

*End results.* These are summarized in Tables V and VII.

Fusion of the involved joints was performed in 9 cases and as a procedure it was 100 per cent successful, proved by physical examination and roentgenogram, but it failed to alter the balance in favor of 3 patients who died of generalized tuberculosis. One uncertain case left the hospital 6 months after operation with solidly fused tarsus but active pulmonary tuberculosis, and has not been heard of since.

*Analysis of mortality.* The entire mortality was in the group with positive sputum.

## TUBERCULOSIS OF THE ANKLE JOINT

There were but 4 cases of tuberculosis of the ankle joint in this series. In 3 of these patients the ankle was the only joint involved while in one of them the subastragaloid joint was also infected.

TABLE \I —MORTALITY IN THE VARIOUS AGE GROUPS IN 210 PATIENTS WITH VARIOUS TYPES OF JOINT TUBERCULOSIS

	Total	Died	Mortality per cent
1-10	48	7	14.8
11-20	46	10	21.7
21-30	52	24	46
31-40	28	10	35.7
41-50	26	5	15
51-60	9	3	33.3
Over 60	1	0	0
Total	210	59	28.5

These 4 were equally divided between right and left feet but the males outnumbered the females 3 to 1.

*Age.* Three of the patients were in the second decade and the remaining one was 58 years of age. The average age at onset was 25 years.

*Duration of the disease.* The duration of the disease was less than 1 year in 3 patients and the other patient had had the disease for 2 years.

*Diagnosis.* The diagnosis was made by physical examination and roentgenogram and was proved correct by the excised tissue in all 4 instances.

*Surgical treatment.* Amputation was resorted to in 1 patient and fusion in 3 patients. The operative procedure employed in fusing the ankle joint was as follows: The articular cartilage of the entire ankle joint, including the medial and lateral malleoli, was removed. Into the raw joint surfaces was packed a mass of bone chips from the tibia and the astragalus. A bone graft from the adjacent tibia was placed across the front of the joint from a groove in the tibia to a similarly prepared groove in the astragalus. A plaster-of-paris boot was applied with the foot at an angle of 100°.

TABLE \II —COMBINED END-RESULTS FOR 224 JOINTS INVOLVED

	Excellent		Uncertain		Died		Total
	Num ber	Per cent	Num ber	Per cent	Num ber	Per cent	
Spines	59	54	19	17	32	29	110
Knees	27	61	8	19	9	20	44
Hips	11	44	5	20	9	36	25
Sacro-iliac	6	37.5	3	19	7	43.5	16
Tarsus	9	70	1	7	3	23	13
Ankle	3	75	1	5	0	0	4
Symphysis pubis	1	100	0	0	0	0	1
Upper extremity	8	72	2	18	1	10	11
Total	124	55.3	39	17.7	61	27	224

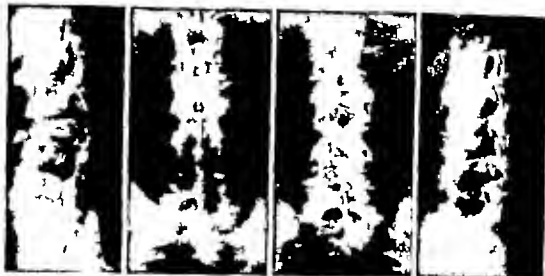


Fig. Case

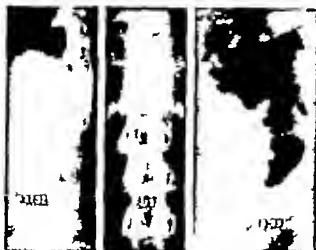


Fig. Case

degrees to the long axis of the leg. The immobilization was maintained for from 4 to 6 months.

**End-result.** The fusion was completely successful in all 3 cases. Three patients rated as excellent had had no evidence of pulmonary tuberculosis. One rated as uncertain has a 100 per cent result as far as ankle fusion is concerned but he has an active pulmonary tuberculosis and is at present in a sanatorium under treatment. He may well achieve an excellent result in time (see Table VII).

#### TUBERCULOSIS OF THE SYMPHYSEAL JUNT

This joint was involved in case 15 in this series, a Greek woman in her early thirties. There was a persisting sinus which had not healed for 3 years. Her general condition was excellent so it was decided to attempt surgical intervention. The diseased bone surface was excised and a bone block from the ilium was inserted into a prepared slot between the pubic bones. A number of chips were added. The block and all the chips extruded as sequestra and the condition cleared up with healing of the sinus and has remained healed and symptomless for 3 years after operation.



Fig 3 Case 3

A simple resection of the diseased soft tissue and the bone would have been infinitely better in this case than the attempted fusion and if there were any subsequent instability, a fusion of the two sacro-iliac joints could readily be done.

This patient had no evidence of pulmonary disease. We have seen tuberculosis of this joint in several other instances but inoperable because of extensive pulmonary disease or widespread dissemination.

#### UPPER EXTREMITY JOINT TUBERCULOSIS

That less than 8 per cent of the total joints involved with tuberculosis were in the upper extremity must be explained on the basis of traumatic incident to weight bearing.

In this series there were 17 patients with upper extremity joint tuberculosis, one having both shoulders affected. In only 5 of these was the upper extremity joint the only one involved. The 12 remaining had various other joints involved. Ten were elbows, 4 shoulders, and 4 carpal or wrist joints.

Of these 18 joints, only 11 were treated surgically. Those not treated surgically at Sea View Hospital included 4 elbows which were terminal manifestations, 1 elbow which had been previously successfully resected, and 1 bilateral shoulder case which also had a hip and spine involved. The shoulder symptoms subsided to a point where they were not considered important enough to warrant operative treatment.

*Age* The highest age incidence was in the second and third decade (see Table VI). The average age at onset was 22 years.

*Duration of disease* The average duration of the disease was 3 years. One patient had an active elbow joint for 15 years. Only 5 of the patients had complained of their symptoms for 6 months or less.

The operative cases were as follows:

1. *Shoulder joint* There were 2 cases, each proved positive by excised tissue. Both had draining sinuses. Both were treated by operative fusion which was successful. The end-result was excellent in both 3 and 7 years after operation respectively.



Fig 4. Case 4



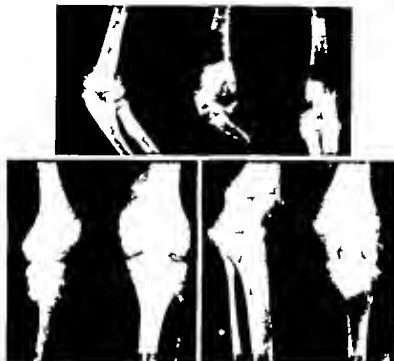


Fig. 5. Case 5.

2. *Elbow joint.* There were 5 cases of elbow joint tuberculosis in this group with a diagnosis proved by tissue examination on 4 of the 5. Sinuses were present in the majority. Fusion of the elbow joint was attempted on all 5. One became solid; 2 developed pseudo-arthritis with quiescent disease; 1 came to amputation and 1 a fungating tuberculous elbow is dying of amyloidosis.

Technically fusion of the elbow joint is difficult in favorable cases and should not be attempted in unfavorable ones. I now believe a careful resection may be a better and more logical procedure in this non weight bearing joint. Our record of only 1 successful fusion in 5 attempts leaves much to be desired.

3. *Wrist and carpal joints.* There were 4 cases of wrist or carpal joint tuberculosis, all proved positive by excised tissue.

Fusion was performed in 3 with excellent results and solid bony fusion though one required a subsequent operation because of prolonged suppuration. The one failure patient died of an embolus 3 days after operation.

*End-results.* These are summarized in Tables V and VII.

The mortality in this group is low but the 2 uncertain cases will probably raise it.

#### CASES WITH MULTIPLE JOINT FOCI

There were 43 patients who presented multiple tuberculous joint, tendon sheath and bone, foci. Among these 43 patients were 113 separate foci, 64 of which were operated upon at San View Hospital, elsewhere and 37 foci were inoperable.

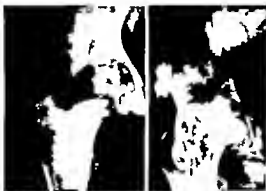


Fig. 6. Case 6.



Fig 7 Case 7



Fig 8 Case 8

being either terminal or quiescent manifestations (see Table X)

Eighty per cent of the patients were under 30 years of age (see Table VI). The average duration of disease was over 4 years though 2 cases had persisted for 33 years or more, 4 others over 10 years. Only 6 had symptoms for 6 months or less.

Twenty-five of the patients had spinal involvement. Nine patients had sacro-iliac involvement, which as has been shown, carries with it a very bad prognosis. Of 14 fatal cases in this group, only 2 were worthy of attempt at salvage by operation on a second focus.

**End-results** These are summarized in Tables V and VII.

Even with this massively involved group of cases, when the derelicts are excluded, such as one patient who had a second spine focus, dactylitis, tendon sheath and rib involvement, the results were surprisingly good in those patients chosen for operation.

Of the 10 patients in this group who had two or more joints operated upon, 70 per cent had excellent results over 5 years after operation (Table VII).

The 7 excellent results include some of our most brilliant and satisfactory cases. They are as follows: (1) a spine and sacro-iliac joint, (2) a right knee and left hip joint, (3) a carpus, tarsus and spine, (4) a spine and hip joint, (5) a shoulder, sacro-iliac and spine (2 foci), (6) a knee and elbow joint, (7) a knee and carpus. All of these joints are solidly fused and the patients are well and out of the hospital.

One of these patients had pulmonary tuberculosis with positive sputum, 4 had pulmonary tuberculosis with negative sputum but had meta-

static spread to other organs. One had negative sputum with no metastatic spread. Only 1 patient of the 7 had no evidence of pulmonary disease.

These excellent results make us reluctant to condemn every patient with positive sputum or metastatic spread. They are brands snatched from the burning.

#### SUMMARY

Involvement of the joints is a serious manifestation of tuberculosis. It is essentially a disease of early adult life. The average age of onset for these 210 patients was 22 years. The mortality among these patients was 28.5 per cent and will undoubtedly be higher as time goes on and the number of deaths is augmented from the list of those we consider as uncertain. In the first decade of life the mortality in this group was only 14.8 per cent but in the third decade the disease took an enormous toll of our patients, as the mortality mounted to 46 per cent (see Table XI).

From the surgeon's standpoint the treatment of this disease is beset by many disappointments which are offset by the restoration to a relatively normal life of a majority of the patients. The operative treatment in joint tuberculosis aims to eliminate, by amputation, a dangerous focus which cannot be saved, or to attempt to heal by putting the involved joint at complete rest by operative fusion. In this latter case the surgeon merely creates a more favorable situation for healing and the patient recovers if the balance is thereby turned in his favor. The statement of Ambroise Paré, "I dressed him, God healed him" (*Je le pansay, Dieu le guarit*)<sup>1</sup> never held more truth than in the treatment of this disease.

<sup>1</sup>Quoted from Garrison's *History of Medicine* 4th ed p 225

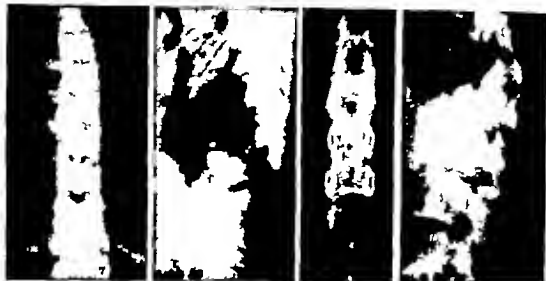


Fig. 9 Case 9

The fate of the patient depends upon the nature and extent of his tuberculosis. Those patients with positive sputum, caseous pneumonic lesions, etc. and those with pulmonary disease negative sputum but with metastatic spread to other organs have shown a mortality of 5 per cent. On the other hand those patients with inactive pulmonary disease and no metastatic spread to other organs and those with no evidence of pulmonary disease have shown a mortality that is only 9 per cent.

Our mortality rate of 47 per cent for patients with active pulmonary disease (caseous pneumonic tuberculosis (see Table V, Group A)) should be compared with the mortality in similar cases uncomplicated with joint manifestations.

David Ulmar reports, in a personal communication, that at Metropolitan Hospital, New York City of 700 consecutive admissions with caseous pneumonic tuberculosis, 68 per cent died within a year and at the end of a 10 year period less than 1 per cent survived.

From the Rhode Island State Sanitarium, Barnes and Barnes have reported a death rate for patients with tuberculosis showing cavities in the lungs of 80 per cent within a year of admission.

A consideration of these facts amply explains the high mortality in those patients in this series with active pulmonary disease.

Another factor which adversely influences the end result is prolonged suppuration from sinuses with resulting ankylosis disease.

The only joints in our experience which tend to fuse spontaneously are those of the spine. This occurs only in 1 per cent of the cases and then only after many years and tremendous deformity has ensued.

A study of the combined end-results of the 214 joints treated show the following facts (see Table VII). The upper extremity joints, tarsal and ankle joints had the highest percentage of excellent results, each group 70 per cent or better. The knee joint cases showed 61 per cent and the spine cases 54 per cent excellent results. The percentage of excellent results fell to 44 per cent in the hip joint cases and to 37.5 per cent in the sacro-iliac joint cases. As the excellent results declined, the mortality rose. The sacro-iliac joint with a mor-



Fig. 10 Case 10

ality of 43.5 per cent is, in our experience, the gravest form of joint tuberculosis while the knee joint and upper extremity joints offer the best prognosis.

The work in this series of patients is almost entirely salvage. They represent a selected group, selected from the standpoint of probable unfavorable outcome. Coming from the lower classes of society, from poverty and disease, of less vital strains, they have been discarded by most of the city's hospitals and sent to Sea View Hospital for ultimate disposal. This is joint tuberculosis such as is not usually reported. The 300 odd cases which we rejected as unsuitable for surgery, presented the appalling mortality of over 80 per cent.

Our results in these 224 operative joints showed 124, or 55.3 per cent, which can be honestly rated as excellent, 39, or 17.4 per cent, uncertain, and 61, or 27.2 per cent, died. The fact that only a little over half can be rated excellent should not be considered remarkable but what should be stressed rather, is that so many patients can be salvaged from such an unfavorable group.

#### CASE REPORTS

The following 10 case reports, in brief abstract, with roentgenograms are submitted as typical of varying phases of the problems encountered in these 210 patients.

**CASE 1. C. F.** A young woman of 23 years with a history of backache of over 1 year's duration (Fig. 1). The pre-operative roentgenograms show definite destruction of the second and third lumbar vertebrae. A spine fusion was done extending from the twelfth dorsal to the fifth lumbar inclusive. Postoperative course was quite uneventful. The spine was solidly fused clinically 6 months after operation and the roentgenograms taken 10 months after operation prove this solid fusion. This patient had no evidence of pulmonary involvement and was discharged as an excellent result 10 months after operation.

**CASE 2. M. C.** 61-28. A young woman of 25 years who came to Sea View Hospital in 1926 (Fig. 2). She gave a history of pleurisy 6 months before admission and shortly after this she developed a painful swelling of the right shoulder.

A diagnosis of tuberculosis of the shoulder joint was made and at time of operative fusion in November, 1926, tissue removed confirmed the diagnosis. She had an occasional positive sputum. In November, 1927 she developed a lesion in the spine, involving the twelfth dorsal and first lumbar. This area was operatively fused in February, 1928. The left sacro-iliac joint was next invaded and operatively fused. The patient left the hospital and has been home well for 4½ years. When she last appeared for follow up examination in February, 1933, a small kyphos was found above her former spine fusion and she complained of a little mid-dorsal backache. The roentgenogram showed a lesion involving ninth and tenth dorsal vertebrae.

These roentgenograms taken in 1933 show a fused shoulder joint, a fused dorsolumbar spine, and a fused left sacro-

iliac joint and the latest focus involving the ninth and tenth dorsal vertebrae which has subsequently been fused. Attention is directed to the solidity of the lumbar spine fusion 5 years after operation. The pre-operative roentgenograms were destroyed along with other inflammable films several years ago.

This is shown as an example of diffuse spread, with multiple joint lesions in a patient whose resistance is very high. Her general condition is excellent.

**CASE 3. G. H.** 5122-31. A man of 37 years who since the age of 4 years has had tuberculosis of the spine with tremendous deformity resulting. He came to Sea View Hospital in 1931 with a 10 year history of painful swelling in the right knee. This was diagnosed and at operation proved to be tuberculosis. A knee fusion was done in November, 1931, and also the tendon sheath of the right middle finger was excised as he had a proved tuberculosis of this sheath.

This patient was discharged from the hospital 6 months after operation. He wore a circular plaster splint for 3 months longer. He has a solidly fused knee joint and is in excellent condition 2½ years after operation.

The roentgenograms show the right knee before operation in October, 1931, and after operation in July, 1932, (Fig. 3).

**CASE 4. W. R.** 3166-30. This patient, a boy of 17 years with active pulmonary disease and positive sputum, came to Sea View Hospital in 1929. He subsequently developed a painful swelling of the left ankle joint. This was diagnosed tuberculosis. A fusion of the ankle joint was performed in May, 1930, and the tissue removed confirmed the diagnosis. The fusion was solid and patient was walking without support 9 months after operation.

His pulmonary disease has been treated with pneumothorax and sputum has been negative. He is still under treatment for pulmonary tuberculosis at Otisville Sanitarium, with a very good prognosis.

The roentgenograms show the ankle joint in April, 1930, before operation and in January, 1931, after operation (Fig. 4).

**CASE 5. H. F.** 20-30. A colored boy of 11 years who came to Sea View Hospital in 1928 and who developed pain and swelling in the left knee and a little later in the right elbow. These complaints were noted subsequent to his admission to hospital for a non-productive cough and loss of weight. He also had a keratitis. His general condition improved steadily. His sputum was scanty and always negative.

In March 1929 the knee was operatively fused and the elbow was similarly treated in July 1929. Tissue removed at both of these operations confirmed the pre-operative diagnosis of tuberculosis. Both operations were successful. The knee joint, however, bent through the epiphyseal line into recurvatum and had to be straightened with an osteotomy of the femur. The patient is in excellent condition at home with both joints solidly fused, 5 years after operation.

The roentgenograms show the elbow joint in July, 1928, before operation and in September 1931, after operation and the knee joint in June, 1928, before operation and in October, 1930, after operation (Fig. 5). Attention is directed to the solid bony fusion of the knee joint with the recurvatum deformity which occurred through ununited epiphyses.

**CASE 6. C. M.** 4513-31. A colored girl of 12 years who was admitted to Sea View Hospital in 1931, complaining of

pain and stiffness in the left hip for 8 months prior to admission. A diagnosis of tuberculosis of the hip was made and subsequently confirmed by tissues examined. A fusion of the hip joint was done in May, '03. A large mass of disc bone was used as graft from the femur to the ilium. The patient wore double plaster of paris spica bandage for 4 months and then single spica. She began to bear weight 5 months after operation and 18 months all support was removed and fusion was definitely solid.

The patient had no evidence of pulmonary tuberculosis. She has been home over year and continues well, an excellent result 7 years after operation.

The roentgenograms show the left hip before operation in May, '03 and after operation in May, '04. Excellent bony fusion (Fig. 6).

CASE 7. M. B., 77-38. An Italian girl of 6 who was admitted to Sea View Hospital in '02 with extensive tuberculosis of the spine and of the right hip joint. The spine was explored and spontaneous fusion was found from seventh dorsal to second lumbar. Four vertebrae above and below were added because of the severity of the kyphosis and extent of the disease. In August, '07, hip fusion was done, an iliac graft being used to bridge the gap from the femur to the ilium. Tissue removed confirmed the diagnosis of tuberculosis. A plaster spica was worn for 6 months and, during the last month of this period, the patient began to bear weight. She left the hospital 9 months after operation. When seen in follow up in 1933, 6 years after her hip fusion, her general condition was excellent, hip was solidly fused.

The roentgenogram taken in '03 shows solid fusion of the right hip (Fig. 7). Her pre-operative pictures were destroyed because they were unobtainable film.

CASE 8. A. C. 93-28. A boy of 7 years, admitted to Sea View Hospital in September, '03. He had been in various hospitals for 3½ years because of pain and stiffness in his left hip and later his right knee. There was active disease in both these joints. In March, '06, fusion of the right knee was performed and in April, '06, fusion of the left hip was performed. Tissue removed at each of these operations showed tuberculosis. He wore circular plaster on the right knee for 6 months. New fusion was found to be solid and the hip joint was supported by plaster spica for 8 months, at which time the joint was definitely fused. He was discharged from the hospital 10 months after operation in excellent condition, and has remained well, an excellent result, 7 years after operation.

The roentgenograms show the end result of the hip and knee in March, '03 (Fig. 8). Pre-operative films are destroyed. The patient is shown as an excellent result in multiple foot cast, the patient previously having had 3½ years of constant treatment, at the end of which period he was bedridden with active disease in both hip and knee joint. This boy has grown tremendously since operation and the involved joints that were fused have kept pace with the uninvolved joints.

CASE 9. E. G. 907-28. A woman of 24 years, admitted to Sea View Hospital first in '06 and again in '05 for pulmonary tuberculosis. She had an active pulmonary lesion with positive sputum until March, '00. From that date until her discharge from hospital in October, '02, her sputum was negative. She developed lower dorsal back ache and slight kyphosis while under treatment for pulmonary tuberculosis. In September, '00, definite disease was noted by X-ray in eleventh and twelfth dorsal vertebrae and spine fusion was done extending from ninth dorsal to second lumbar.

Postoperative course was uneventful. The patient left the hospital 3 months after operation with solidly fused spine and her pulmonary condition arrested.

The roentgenograms show the lesion in eleventh and twelfth dorsal before operation, July, '00, and 3 years after operation in September, '03. Bony fusion was readily seen and fusion of the bodies is taking place (Fig. 9).

CASE 10. N. L. 33-27. This patient, female infant, was admitted to Sea View Hospital at the age of 6 months because her mother was patient with pulmonary tuberculosis. The mother died of her disease. This little patient had active pulmonary disease and cold abscess of the left thigh. Her earliest roentgenograms showed erosion of the femur and tissue from the abscess cavity showed tuberculosis. The left hip joint became involved by direct extension from the femoral shaft.

A fusion of the hip joint was performed in January, '06. Her patient was 3 years old. This fusion was clinically solid 10 months after operation. For the past 3 years she has had no symptoms. She is in excellent condition and her fused hip allows her to run around it all.

The roentgenograms show marked cavitation of the femoral shaft and acetabulum before operation in the pre-operative view of December, '00, and the postoperative view of August, '03, show solid fusion across the gap with recalcification of the femur and ilium. An excellent result in seemingly hopeless case (Fig. 10).

## MEDICAL TREATMENT OF AMEBIC INFECTIONS OF THE LIVER

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THE hepatic complications of intestinal amebiasis include acute hepatitis and abscess. Acute hepatitis results in the occurrence of chills, sweats, fever, leucocytosis, and swelling and tenderness of the liver. These symptoms constitute the earliest response to invasion of the liver by *Endameba histolytica*, but, being non-specific in character, they rarely lead to a correct diagnosis even during an epidemic of amebiasis. When correctly diagnosed the treatment is everywhere regarded as being a purely medical problem. Delay in instituting medical treatment permits an increase in the size of multiple areas of softening which may fuse or coalesce to form one or more abscesses. The symptoms of the stage of abscess do not differ materially from those of the stage of hepatitis. The physical signs, however, may show immobilization or deformity of the diaphragm, displacement of the liver, or the presence of a mass in the upper abdomen or right lumbar region. The treatment for this stage of amebic infection, unlike that of hepatitis, is almost everywhere surgical. Craig says, "The treatment of amebic abscess of the liver is largely a surgical problem, but as already mentioned the early recognition and treatment of amebic hepatitis and beginning abscess formation is essentially a medical problem." In a recent article, Freund expresses the belief that immediate operation is important in the treatment of amebic abscess of the liver.

That a pyogenic abscess is best treated by surgical measures is not subject to dispute, but a pyogenic abscess and an amebic abscess are not comparable conditions. An amebic abscess is the result of the lytic action of ferments liberated by amebas. The material in an amebic abscess is composed of liquefied liver tissue and red blood cells in various stages of disintegration. Cells of leucocytic origin are not found in an uncomplicated amebic abscess, nor are living amebas present in the material first evacuated, although they may be present in great numbers in the tissue which forms the wall of the cavity. It is by reason of their location in the wall of the cavity that they are enabled to continue their lytic action, thereby constantly enlarging the size of the abscess. An amebic abscess differs from a pyogenic abscess further in that it is caused by a parasite that is easily killed by any one of several drugs introduced into the body at a point remote from

the actual site of infection. In view of these facts, surgical evacuation of an amebic abscess of the liver would appear to be an illogical procedure.

Surgical drainage of amebic abscesses of the liver is attended with an extremely high mortality rate, particularly when an open operation is performed. The danger of open operation resides in the fact that secondary bacterial infection is an almost invariable sequel. In 75 of 87 cases of liver abscess reported by Rogers, cultures for pyogenic bacteria made at the time of operation were sterile, although subsequently bacterial infection occurred. Aspiration is less likely to result in secondary bacterial infection since it does not leave an open sinus, but this advantage is almost counterbalanced by its own peculiar shortcomings. Aspiration is an attempt to introduce the point of a needle into a cavity of unknown size, at an unknown depth in the largest organ in the body. Should the needle enter the abscess at the first attempt only a fraction of the sterile liquid contents could be aspirated, and even if the abscess could be evacuated completely, the parasite which caused it has not been disturbed, since it is situated at varying depths in solid liver tissue. Failure to strike the abscess at the first attempt is likely to cause dissemination of the infection throughout the liver as a result of implantation by multiple punctures. I have seen such induced abscesses on several occasions at autopsy. With both open operation and aspiration too much reliance is placed on the assumption that amebic abscesses always occur singly. Numerous instances of multiple abscesses have been reported. Wherein lies the advantage of partially evacuating an amebic abscess, or even evacuating it completely, if another abscess exists that has not been drained? Gesner has collected and reported 56 cases of amebic liver abscess. In 23 cases the abscess was incised and packed with iodoform gauze, in 17 cases the abscess was incised and drained with tubes. In each group there were 5 deaths. Cort reports 530 cases of amebiasis in 97 of which there was hepatic involvement. In 14 cases the abscess was evacuated by aspiration, in 2 by rupture through the lung, and in 1 by rupture into the pleural cavity. The remaining cases were treated medically. He says, "In all cases the injection of emetine brought about amelioration of symptoms and reduction in the size of the liver within 2 to 4 days. In

some cases this reduction was almost incredible. There was only 1 death in the entire series and this case had cardiorespiratory findings. Cost for operation only when there is a secondary infection. Murray and Koh report 23 cases of amebic liver abscess, in 2 of which treatment was by emetine alone. Biggam and Chahouni report 25 cases treated medically for from 5 to 7 days as a preliminary to aspiration. In 2 of their cases recovery was so prompt that aspiration was not necessary. Manson-Bahr reports 45 cases of amebic liver abscess in 13 of which cure followed medical treatment with emetine and emetine bismuth iodide.

As a result of the epidemic of amebiasis which occurred in Chicago I had the opportunity of treating 2 cases of amebic liver abscess. Convinced of the dangers of surgery in this condition and convinced that surgical treatment of an uncomplicated amebic abscess is illogical, both cases were treated medically.

CASE. F. W. white male, aged 50 years, referred by Dr H. E. F. Barnard, was admitted to Wesley Memorial Hospital November 27, 1931. His illness of 6 weeks duration was initiated by signs of an upper respiratory tract infection followed in 3 weeks by pain and tenderness in the lower right chest and under the right costal margin. The pain was associated with chills and fever. The sequence of events and the physical findings suggested the possibility of pleural effusion and diagnostic thoracentesis had been done. His sputum results. On admission examination revealed presence of the right lower region with marked tenderness on palpation and percussion. A spherical mass extending downward and forward from beneath the liver could be felt. The lateral margin of the liver was an inch below the costal margin. The chest showed partial right pneumothorax. The white cell count varied between 10,000 and 15,000 and the temperature between normal and 104 degrees for the first week. The urine was normal. The stools did not contain either trophozoites or encysted forms of *E. histolytica* until after the administration of saline cathartic. X-ray examination confirmed the presence of partial right pneumothorax and showed fixation of the right diaphragm. Treatment with emetine hydrochloride was instituted on November 5. The last febrile reaction of 99 degrees occurred November 20. On the day of discharge, December 7, neither the mass nor the liver could be felt and all pain and tenderness had disappeared. The past history of the patient indicated the possibility of amebiasis of

years' duration with latest period of 3 years immediately preceding development of the liver abscess.

CASE. J. J. S. white male, aged 30 years, referred by Dr. Ira Greenberg, was examined on March 1, 1934. The illness for which he sought relief began acutely on January 3, 1934 with fever, chills, severe pain in the right side of the abdomen. There followed loss of weight, weakness, and an increase in the pain which had become unbearable. Examination showed emaciation, pallor, a subcostal tenderness to the right and prominence of the right upper quadrant of the abdomen. The liver edge was 10 centimeters below the costal margin and was distinctly tender. The spleen could not be felt. White blood cells 12,000, red blood cells 4,000,000, hemoglobin 58 per cent. The urine was normal. A blood culture remained sterile. Wasmann's and Kahn's tests were negative. Examination of the stools was negative until after the administration of saline cathartic. Motile amebae and the Trichomonas trophozoites were then found. Treatment with emetine was instituted. Recovery was gradual with disappearance of all symptoms and signs after April 1, the last day on which there was any elevation of temperature.

#### CONCLUSIONS

Uncomplicated amebic infection of the liver whether in the stage of acute hepatitis or of abscess can be treated successfully by medical measures alone. Surgical treatment should be reserved for cases complicated by secondary bacterial infections and for other complications, such as rupture of the abscess into the pleural or peritoneal cavities.

#### BIBLIOGRAPHY

1. PROHAM, A. G. and GRILLON, VOL. I, P. Amebic liver affecting symptoms and treatment, with review of 3 cases. *J. Trop. Med. & Hyg.* 41: 26 1937.
2. COST, E. C. Abscesses of the liver. *J. Am. M. Ass.* 94: 90 1905.
3. CHAM, CHARLES F. Abscesses and Amebic Dysentery. P. 208. Springfield, Ill. Charles C. Thomas, 1934.
4. FAY, H. A. Amebic abscess of the liver. *J. Am. M. Ass.* 914, 590-55.
5. GRAY, H. B. Abscess of the liver. *Am. J. Surg.* 93: 20 1903-04.
6. MA, W. B. Amebic abscess of the liver its diagnosis and treatment. A clinical study. *Proc. Roy. Soc. Med.* 19: 5, 33.
7. MIRA, FERNANDEZ J. and KOW, P. K. Amebic liver abscess. *Canadian M. Ass. J.* 40: 263.
8. ROBINSON, BEN J. Amebiasis. On amebic liver abscess its pathology, prevention and cure. *T. Med. Soc. Lond.* 1924: 45, 30-9.

## PINEAL TERATOMAS

WITH REPORT OF A CASE OF OPERATIVE REMOVAL<sup>1</sup>

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PINEAL tumors are considered to be of extreme rarity, and to constitute but 0.7 per cent of all intracranial tumors (5), which latter in turn are the cause of only 0.06-0.15 per cent of general mortality (20). Even within the assembly of tumors of the pineal gland, however, teratomas are rare, only 25 have been reported in the literature of the past half century, the case presented herein, a teratoma, is possibly unique in its range of histologic structure. Tumors of the pineal region are not only difficult to diagnose (only about 30 per cent of those reported in former years were diagnosed clinically), but even when antemortem diagnosis has been possible, therapy has been considered hopeless. It is true that misdirected cerebellar operations have at times been undertaken (5), but surgery's attitude toward purposeful operative attack upon these tumors has been (Cushing, 1926, 4) that "it is improbable that we shall ever be able successfully to extirpate these lesions, in view of their inaccessible position from all points of view they are most unfavorable." Such a therapeutic impasse is always a challenge to endeavor, however, and in the past decade and a half surgical resource and daring has on 6 occasions successfully accomplished the removal of such tumors.

## REPORT OF CASE

D F, a boy aged 6 years, was referred for examination September 20, 1932, by Dr Thompson Coherth The Dalles, Oregon with complaints of headaches, vomiting and failing vision.

His birth had been at term, with normal labor but it had required 35 minutes to induce spontaneous breathing. He was jaundiced for 8 or 10 days in the first month of life, pus was expressed from his tonsils when he was 2 weeks old. He had "influenza" at 4 months and at 6 months, and a bilateral pneumonia when 9 months of age, a cervical lymph gland on the left side was drained when he was 1 year old. He had had almost continuous coryza each winter. He had pertussis when 2 years of age, measles when 4 and again when 6 years of age, with the last attack a myocarditis had been diagnosed and his parents had spent several weeks in the mountains with him, preliminary to a contemplated removal of tonsils almost occluding his pharynx. He had been subject to colic like attacks during the first several months of life, he had had considerable trouble with his teeth, his appetite was fickle and he was chronically constipated requiring laxatives several times a week. Cardio-respiratory and genito-urinary history was negative. He was precociously bright at home, had always been restless in his sleep. His gait was normal and he "ran like a deer."

His best weight had been 40 pounds, 6 pounds under the ideal, but he had recently lost considerably in weight.

For the 3 weeks preceding his present illness he had often had sudden bouts of severe intertemporal and frontal headache with sharp prostrating pains, occurring most often at evening and night, these had been ameliorated by castor oil catharsis. He had become "nervous" (unusually quick) in his movements, his voice had lost its intonation, he had begun to stutter, "after a few minutes' conversation he would be screaming almost at the top of his voice." The right side of his face did not function as well as the left. A week before examination, after being given one aspirin tablet for headache, his vomiting at frequent intervals had begun, emesis relieved his headaches. For 5 days he had had attacks of severe epigastric cramps, bad enough to make him "rave with pain", these spells were apparently independent of the headaches. Three days before examination, his left eye had turned inward, and he had complained of double vision at such times as he could see, light hurt his eyes, and his vision had become foggy, with frequent total obnubilations. For 12 to 14 hours he had complained of pain back of his left ear and high in his neck.

Examination showed a small, dwarf like, well formed boy, with hyperkinetic reactions, and a good coat of sun tan. MacEwen's sign was positive, circumference of head 49.8 centimeters (nor 50.2 centimeters), some sub occipital tenderness, without stiffness of neck. Teeth were carious, tonsils were huge ragged bulbs that almost met in the midline, posterior cervical lymph nodes were enlarged. Thoracic contents, spine genitalia (Fig 2a), and extremities were not remarkable, abdomen was scaphoid, sigmoid gassy, and the lower pole of the right kidney was palpable. Neurologically, left eye and right eye were 20/66 with considerable concentric contraction of fields (3/2000 disc seen only 8 to 10 degrees from fixation point of Bjerrum screen). Bilateral typical choked disc, with 5.0 diopters elevation but without hemorrhages. Paralysis of right abductors, and complete inability to deviate eyes above horizontal, pupils 6 to 7 millimeters in diameter, with normal reactions, left corneal reflex was slightly sluggish. Minor right facial paresis. Remainder of cranial nerves normal. Speech was spontaneously repetitive of sentence fragments (palilalia), and voice a flat monotone. No disturbance of muscular power, nor of any modality of deep or superficial sensation, to objective testing. Tendon reflexes were equal and active in upper extremities but knee jerks were absent bilaterally, and 3 to 4 clonic jerks were present at the left ankle, a positive left Oppenheim was present but no other pathological reflexes. Co-ordination tests showed some dysmetria of the right arm, but no ataxias whatever, minor right dysdiadochokinesia, spontaneous post pointing on the right to the right, considerable hypotonia, marked sway in Romberg position, with listing to the left, gait with normal base but with veering to the left, and ultimate left fall. Cranial roentgenograms showed sutural diastasis, and moderately advanced convolational atrophy, no detectable calcification of the pineal body was present.

The syndrome presented was almost entirely mesencephalic. The supranuclear paralysis of upward movements of the eyes (Parinaud syn-

<sup>1</sup> Presented before the Oregon Pathological Society, Portland, April 23, 1934, and abstracted in Transactions Northwest Med. 1934, 33:216 also presented before the Staff of the Good Samaritan Hospital, Portland, December 9, 1932.



drome) indicated the region of the anterior quadrigeminal bodies, the dysmetria (without ataxia) the monotonous voice the veering and late fall, were primarily affections of the anterior tegmentum, the dyadiadochokinesis past pointing hypotonia, and absent knee jerks were cerebellar symptomatology due to interference with the superior portions of the brachium conjunctivum embedded in the tegmentum, the clonus, facial paresis, and Oppenheim reflex similarly indicated aberrations of motor projection tracts which here traversed this region. In view of the sudden onset of intracranial tension (vomiting choked disc, headache, Macewen's sign, sutural diastasis) a fulminating obstruction of cerebrospinal fluid had occurred, the aqueduct of Sylvius traverses the mesencephalon and is of small caliber. Whether the pathology and central visceral crises were regarded as thalamic or hypothalamic did not much alter localization. Since objective examination gave no support to symptomatology arising from structures immediately adjoining the mesencephalon, glioma was improbable, age made cholesteatoma, and meningioma of the tentorium, unlikely, macrogenitosclerosis praecox appears in only about 40 per cent of pineal tumors in males, and its absence would not speak against pineal neoplasm. Although lateralization was mostly to the right (clonus, tegmental and brachium conjunctivum signs, abduction, Oppenheim) the opposite side was also indicated (post auricular pain, corneal reflex, seventh paresis) this bilaterality would again favor a lesion lying close to the midline.

A diagnosis of pineal tumor was made, and, after the situation and prognosis had been talked over with the boy's parents, he entered the Good Samaritan Hospital September 3, 1913. By this time he was often irrational, and small hemorrhages had appeared about both optic discs, left lagophthalmos was present, with left Oppenheim and Gordon and right Babinski, he was wholly unable to sit upright or to stand unsupported, falling promptly to the right in both instances, no ataxia or dysmetria was then present. He had apneic periods of 5 to 10 seconds' duration in the course of his Cheyne Stokes respiration, his weight was only 34 pounds.

In the absence of operative intervention the ultimate prognosis in pinealomas is so hopeless that direct attack upon the growths would seem warrantable. Palliation might be undertaken by subtemporal decompression and roentgenotherapy (5) but inasmuch as such tumors sooner or later produce an obstructive hydrocephalus either at the iter or at the tentorial incisure, this procedure must necessarily become wholly ineffective ultimately (11) even if initially possible. In the present instance, with a fulminating internal hy-

drocephalus already well established a subtemporal decompression was obviously inapplicable. Suboccipital decompression has uniformly been found promptly fatal except in the fortunate instance reported by Cairns (12) the mechanism of this latter type of fatality is readily perceptible—in the presence of unalleviated hydrostatic tension anterior to the tumor release of pressure in the posterior fossa could serve only to impact more tightly any tissue caught within the embrace of the unyielding tentorial incisure, thus compressing mesencephalic centers even further with consequent decerebrate rigidity, tonic convulsions, intracerebral extravasation and precipitate extirpation as sequelae.

The possibility of direct attack upon the pineal region had been discussed in hortatory generalities in the first decade of this century but 1913 first saw the clinical problem attacked with a practical determination which soon resulted in an embarrassment of dubious riches. Nemeth's parasagittal operation (3) was obviously too unsatisfying for serious consideration. Krave, having had success in removing a quadrigeminal tumor through the posterior fossa, by tracing sublaterally the superior surface of the cerebellum, advocated (13) a similar route for pinealomas but was nevertheless unsuccessful later in outstripping a tumor by this method (16) this exposure is at the bottom of a funnel, is surgically hazardous because of tenuous veins between the cerebellum and tentorium, and furthermore, since most pineal tumors present into the incisure from above, the procedure advances upon the pathological condition from below the impaction, I do not believe the route has since been used. Bremner painstakingly worked out a unilateral transoccipital procedure (19) ligating the sinus anchoring the occipital lobe to the sinus longitudinalis, retracting the lobe, splitting the posterior portion of the corpus callosum, and transecting the tentorium alongside the sinus rectus, thus exposing the entire mesencephalic roof. Various minor modifications and supplements of this approach have been used in practically all successful extirpations since that time, as is shown in Table I. The problem thereafter lay dormant until the World War had passed, when Dandy (6) having

Large parasagittal trepan, resection of sinus ligated side, lobe, and tentorium (partial) resection of hemispheres, destruction of posterior part of the corpus callosum, exposing the pineal region. I was the patient could not receive a resection of the sinus rectus which, though the great vein of Dandy, encompasses much of the material removed from the base of the brain, the resection of the posterior part of the corpus callosum would certainly create a deep, if not a complete, division in the hemispheric connection, and the resectable structure. (Also cited in H. Dandy and L. Schoenbaum: *Chirurgische Leber- und Gallenkrankheiten*, 1922.)

Dandy's original description does not mention the transection of the tentorium. This important step was first mentioned as far as I can determine, by Trendelenburg (21) in 1920.

had difficulty with the transoccipital route in experimental animals,<sup>1</sup> modified Brunner's exposure so as to approach the region by a *transparietal* midline route, bisecting the splenium and transecting the lower part of the falx cerebri, he used this approach to expose one tumor and to extirpate two. In 1931, Van Wagenen (33) published his *transcortical* route, and exenterated a pineal tumor successfully by the procedure.

Four successful extirpations have been accomplished by the Brunner route, one by Dandy's and one by Van Wagenen's. In addition, the Brunner route has been used unsuccessfully (patient not living to be discharged from the hospital) in 4 instances, and in yet another no tumor was disclosed though the operation was carried through successfully and the patient recovered, the route has furthermore been twice used in the same patient to evacuate a glomatous cyst of the quadrigeminal plate (10, Case 33).<sup>2</sup> Dandy's route has been used unsuccessfully in two instances, and in another the result has not been disclosed.<sup>3</sup>

The detailed late postoperative neurological status of patients surviving the operation is found only thrice in the literature (Foerster, Cairns, Van Wagenen). The ataxias, and the extrinsic and intrinsic oculomotor phenomena which follow transiently, may as readily be attributed to release of mesencephalic pressure as to direct operative trauma, the frequent transient hemiparesis may probably be due either to spreading venostatic edema of the occipital lobe, or to unmentioned direct trauma to the vein of Trolard. In the 2 instances in which vision had not been completely lost before operation, a permanent contralateral homonymous hemianopsia has followed operation—attributed in Cairns' case to the necessitous ligation of the internal occipital vein (which drains the area striata—12), and in Van Wagenen's case to the subcortical transection of

the optic radiation in his approach to the ventricle.<sup>4</sup>

Finally, the modern Brunner approach possesses a still further advantage of almost inestimable value, one which has not heretofore been sufficiently emphasized, this occurs incidentally in the course of the operation by the routine performance of what Naffziger (22) has called an "internal decompression," through transection of the tentorium alongside the sinus rectus, thus effectively releasing the internal foothold for counter traction theretofore given the tumor, and, in the presence of infiltrative or irremovable growths, offering surest and most prolonged relief from the torture of an obstructive hydrocephalus.

I am aware of no means other than direct operative exploration which can at the present time determine whether a pineal growth be circumscribed or invasive. With the foregoing considerations in mind, the Brunner procedure was chosen for exploration of the pineal region, after ventriculography had given objective confirmation of the clinical diagnosis.

*Ventriculography*, September 28, 1932, yielded clear cerebrospinal fluid under great tension, but with normal microscopic and serologic findings; the roentgenographic examination showed (Fig. 1) symmetrical internal hydrocephalus without displacement, and a soft tissue mass projecting downward in the midline from the posterior superior portion of the third ventricle. Under procaine anesthesia supplemented by avertin, a left occipital bone flap (Fig. 2 b, c) was turned down with difficulty, due to increased midline vascularity, the patient's condition became poor, the ventricle was tapped to release air and fluid, and the wound closed. The following day, he had a full blown right ophthalmoplegia externa, the only movement possible in the left eye was a few degrees of downward deviation, both pupils reacted normally, but were obliquely ovoid, and were displaced eccentrically toward the nose. No evidence of hemiparesis, bright, alert, rational, but slept much, with Cheyne-Stokes respiration. In 5 days the left eye had regained normal motion, and the right could perform upward and downward movements. Second stage operation was October 5, 1932, four groups of suspending veins spanning the space from the sagittal sinus to the occipital cortex, were ligated or coagulated, one of the groups escaped from its ligature and it was ultimately necessary to use muscle stamps from the gastrocnemius to effect stasis, the wound was again closed. There was subsequent anorexia, intermittent periods of marked motor restlessness, and complete unwillingness to talk. By October 15 his weight had dropped to 18 pounds despite high calorie diet, rectal feedings and intravenous glucose, he was transfused with 225 cubic centimeters of whole blood, and his hemoglobin rose from 65 per cent to 93 per cent.

*Third stage exploration* was undertaken on October 17, 1932. The occipital lobe was exposed, and after the final anchoring vein had been doubly ligated with silk and its tributaries blocked with silver clips, it was divided, the occipital horn was tapped, the lobe protected with saline

<sup>1</sup>It is possible that the bony tentorium in animals was the factor causing his serious difficulties with the veins of Galen.

<sup>2</sup>The route has also been successfully used to biopsy yet another glioma of the quadrigeminal plate by Foerster in 1930 to my personal knowledge though the case has not yet been published. It might be added here that Tandler and Ranzi (37) have also advocated this (Brunner) route, supplemented by a *tentorial dural flap* to expose lesions on the extreme lateral side of the basal mesencephalon—the only known feasible route to this untouchable great cross roads of the nervous system.

<sup>3</sup>In a monograph published since this paper was written (Benign Tumors of the Third Ventricle of the Brain Springfield Ill. C. C. Thomas 1933 p. 171) Dandy has reported 4 cases apparently using the Brunner approach to tumors lying within the third ventricle as well as 9 by his *transparietal* route and 8 by his *transventricular* routes. His illustrations of operative procedure would indicate that in the *transcortical* route he approaches the region by a dural flap having its pedicle at the midline and by ligation of the veins along the sagittal sinus on the inferior-lying half of the brain thus allowing gravity to retract the hemisphere and to drain material outward. The position of patient team, and operator would be awkward but the surgical advantages undoubtedly considerable.

<sup>4</sup>The extent of the hemianopsia (might possibly) be diminished in this latter route by placing the cortical incision obliquely horizontal instead of vertical.

TABLE I.—DIRECT OPERATIVE INTERVENTION IN PINEAL TUMORS

Date	Surgeon	Bibliographic reference	Route	Remarks	Clinical operative result		Complications
					Upper cerebral	Lower cerebral	
1911	Brustert, C.	Die Pathologie und Oxyris histologie der Tumoren der Zerkleinerung H. Karschsch. Beitr. Klin. Chir. 1913, 251-4	Kranium	Died post operation	Recovery		Treatment of tumor of brain and hydrocephalus
1911	Penney, L.	Die operative Entfernung eines Cyste der Linsenhöhle pineale. Monat. Chir. 1911, 1912, 1913	Kranium	Excision of cyst	Died few hours later		
1911	Handy, W. E.	An operation for the removal of pineal tumors. Surg. Gynec. Obst. 1911, 15, 2-14	Handy	Indistinct picture of tumor, but excision of tumor			
	Died		Handy	Removal of hard tumor of pineal, 1.5 cm		Died after operation	
	Died		Handy	Correlation of the tumor with the pineal gland	Died in shock		
1912	Chadwick, R.	Pineal pathology. Surg. Gynec. Obst. 1912, 15, 2-14	Kranium	Shunt by the lateral ventricle and the tumor of pineal gland	Died few days later		
1914	Smith, L.	Diagnosis and Treatment of Brain Tumors. St. Louis, C. Mosby Co. 1914, 174	Suboccipital	Cystic tumor removed, size of pineal, pinealoma	Alive 24 months		Memorandum of tumor of pineal gland, after operation, tumor not given
1914	Kramer, J.	Operative Entfernung der Pinealdrüse. Monat. Chir. 1914, 1915, 1916	Kranium	Tumor of pineal gland, size of pineal, pinealoma	Recovery		
1917	Farrar, O.	Die operative Entfernung der Pinealdrüse. Monat. Chir. 1917, 1918, 1919	Kranium	Excision of tumor of pineal gland, size of pineal, pinealoma	Alive 24 months		Eyes deviated right of tumor, blind, left eye paralyzed, no pressure on optic chiasm
1918	Van Wageningen, W.	Operative Entfernung der Pinealdrüse. Monat. Chir. 1918, 1919, 1920	Van Wageningen	Tumoral pinealoma, size of pineal, pinealoma	Alive 24 months		Tumoral left brain, no tumor, no pressure on optic chiasm, no pressure on optic chiasm
1919	Allen, H. W. B.	Diagnosis and Treatment of Brain Tumors. St. Louis, C. Mosby Co. 1919, 174	Kranium	Tumoral pinealoma, size of pineal, pinealoma	Alive 24 months		Eyes deviated right of tumor, blind, left eye paralyzed, no pressure on optic chiasm
1920	Allen, H. W. B.	Diagnosis and Treatment of Brain Tumors. St. Louis, C. Mosby Co. 1920, 174	Kranium	Tumoral pinealoma, size of pineal, pinealoma	Alive 24 months		Eyes deviated right of tumor, blind, left eye paralyzed, no pressure on optic chiasm

TABLE I—DIRECT OPERATIVE INTERVENTION IN PINEAL TUMORS—Continued

Date	Surgeon	Bibliographic reference	Route	Remarks	Clinical operative result		Sequelae
					Unsuccessful	Successful	
1913	Allen S S	Ibid Case 7	Brunner	Adenocarcinomatous teratoma size of walnut	Died 2 1/2 months post-op.		Stupor for 14 days left hemiparesis improved, but sudden failure. Post mortem softening of quadrigeminal lamina and marked cerebral edema
1933	Bailey P	Intracranial Tumors pp 333-336 Springfield Ill C C Thomas 1933 pp 333-336	Dandy	3 by 7 cm teratoid oblique from lateral recess to occipital lobe medial third removed by bilateral operation	Survived 9 days		Pre-operative decerebrate status ameliorating after operation
1934	McLean A J		Brunner	Circumscribed parapineal teratoma	Died in few hr		

Described as (personal communication) consisting mostly of connective tissue, with islands of epithelial cells sometimes forming cysts. The situation and histological description of this teratoid would seem to make it not unlikely that it arose from remnants of the fiber of Reissner which except in normal adult humans extends from the subcommissural organ to the filum terminale of the cord through the central canal (15)

cotton and gently retracted upward from the falx and tentorium by a broad ribbon retractor thus exposing the straight sinus and the vein of Galen (Fig 3). The brain stem was found tightly compressed within the incisure of the tentorium. The presenting posterior 2 centimeters of the splenium were transected, with subsequent persistent escape of clear cerebrospinal fluid, no sign of tumor. The tentorium was incised outward for 3.5-4.0 centimeters alongside the sinus rectus, up to the point of two large transverse venous tributaries. When the tip of this flap was retracted upward, the exposed arachnoid cistern overlying the pineal region was seen to be gray and thickened, the portions nearest the junction of the vein of Galen and the straight sinus bore a number of grouped pin head sized, whitened thickenings, which resembled arachnoid tubercles. The arachnoid was incised, exposing both large lateral tributaries of the great vein of Galen. Underneath this lay still another arachnoid layer and when this latter was also incised there lay exposed (Fig 3) the left lateral pole of a comparatively smooth edematous, grayish yellow tumor, estimated to be about 28 millimeters in diameter. The flattened left branch of the vein of Galen was adherent to this mass and was dissected free with scissors without injury to the vein. Traction on the exposed pole of the tumor with pituitary rongeurs showed it probably movable. A portion about a half centimeter in diameter was removed for biopsy, and the dissection continued medially. Inasmuch as the tumor seemed to deliver well traction was continued and a further segment, probably representing a third of the total tumor was thus obtained. These test explorations showed practically no bleeding and had disturbed the patient but little though his blood pressure was now reported as unobtainable his pulse remained at 140 and his respirations were good. Gentle intermittent traction was applied to the remaining portion of tumor and some final dissection done with patties about the two lesser veins of Galen, which were stretched bloodlessly tight over the top of the tumor. As cautious tractive pull was carried directly laterally, a rounded mass about 18 millimeters in diameter was slowly delivered from under the intact taut veins (Fig 4). During the latter part of this delivery the patient had an oculogyric crisis and his respira-

tions stopped for several seconds, but were quickly resumed spontaneously. There was a minimal amount of venous bleeding from the bed of the tumor on the right, but this was readily controlled by placement of warm saline patties, total amount of bleeding here was probably not more than 3 to 4 cubic centimeters, the tumor bed was left entirely dry, the collapsed occipital lobe lowered into place, floated up with warm saline and the wound closed in the usual manner during the next 55 minutes. Despite stimulants (caffeine adrenalin) and glucose his blood pressure remained unobtainable in the brachial artery, though his femoral pulse remained constantly regular at 120 per minute and his respirations 22 per minute.

An hour and a half after delivery of the tumor and as final scalp sutures were being placed his respirations were 12 per minute and labored, though femoral pulse was still 120 per minute. Despite intravenous lobelin, artificial respiration warmth and intracardiac adrenalin, the patient's heart action ceased at 4.20 p.m., 1 1/4 hours after completion of closure, and 3 hours after delivery of the tumor.

Complete necropsy was obtained (G S Path 865), there were no significant somatic changes, careful microscopic studies were made of pituitary, thyroid, thymus, adrenal, pancreas, and testis, without detection of any departure from normal. The brain was fixed in 10 per cent formalin and examined, the operative field was in good shape, the occipital lobe showed no gross evidence of trauma, and the tumor bed was without hemorrhage, though tissues were slightly stained (Fig 5). Hydrocephalic dilatation and atrophy existed only anterior to the entrance to the Sylvian aqueduct. A normal but flattened pineal body, 3 by 4 by 6 millimeters in diameters was found (Fig 6) pushed downward and backward to the right, lying in apposition and just lateral to the

TABLE II—REPORTED PINAL TERATOMAS

Year	Author	Age	Sex	Reference
1873	Wingart, F.	14	M	Die Lehre von den Tumoren der Thalamische. Arch. f. path. Anat. 1873, 44, 111-129
1876	Falkner, E.	26	M	Ein Chondrocytome im dritten Ventrikel. Arch. f. Path. path. Anat. 1876, 75, 120-123
1887	Coca, J.	12	M	An unusual tumour with cartilage originating in the pinal gland. T. Path. Soc. Lond. 1887, 36, 44
1889	Gandover, L.		M	Zur Genetik der Ektodermis. Sitzung Des. Gesellsch. 1889
1890	Colson	8	M	Ein Tumor des Zirkelhirns, Kempten, 1890
1890	Ogle, C.	16	M	Sarcoma of the pinal. T. Path. Soc. Lond. 1890, 1-4
1890	Ostreich and Shuryk		M	Encephaloma und Ektodermis. Arch. f. path. Anat., 1890, 137, 475
1890	Monnens, P.	27	M	Ein neuer Fall von Tumor des Zirkelhirns. Sitzung Des. Kempten, 1890
1890	Friedl (Hochwart)	1	M	Ueber Drogen der Ektodermis. Deutsche Zeitsch. f. Chirurg. 1890, 31, 475
1891	Boley and Jelliffe	13	M	Tumors of the pinal body. Arch. Int. Med. 1891, 857-860
1891	van der Kerk and van Hout	8	M	Tumour glandulae pinalis et epiphysae cranii. Med. Tijdsch. Genoot. 1891, 1177
1891	Hörner	19	M	Tumour des Zirkelhirns. Monatsch. med. Wochenschr. 1891, 46, 898
91	Tobias	20	M	Die Erkrankungen der Epiphyse. Kritisches, 1891, 101
1891	Falkner	19	M	Ueber den Tumor der Glandula pinalis. Sitzung Des. München, 1891
1891	Schmuck	16	M	Ueber den Tumor des Zirkelhirns. Monatsch. med. Wochenschr. 1891, 46, 1043
1891	Died		M	Ueber den Tumor des Zirkelhirns. Monatsch. med. Wochenschr. 1891, 46, 1043
1891	Ostermann	10	M	Zur Diagnostik der Ektodermis. Sitzung Des. Bonn, 1891
1891	Boley, E.		M	Ektodermis und pinalis. Friedl. Zeitsch. f. Path. 1891, 44, 127
1891	Friedl	20	M	Ektodermis im ersten jugendlichen Mann. Med. Wochenschr. 1891, 27, 300
1891	A. Huprecht, W.	17	M	Tumore des Zirkel, brennendes aus Adenomen. Zentralbl. f. allg. Path. path. Anat., 1891, 30, 917
1891	Lutz, H.	1	F	Zur Diagnostik der Ektodermis und der Kärte der zirkelischen Adenome. Deutsche Zeitsch. f. Chirurg., 1891, 36, 127
1891	Horn and Boley		M	Tumors of the pinal body. Arch. Neurol. & Psychiat. 1891, 12, 430-441 (Case)
1891	Idem		M	Pinal pathology further studies. Arch. Neurol. & Psychiat., 1891, 12, 441-447
1891	Allen, J. S. and Lovell, M. W.	19	M	Tumors of the third ventricle. Arch. Neurol. & Psychiat., 1891, 12, 448-456 (Case)
1891	Allen		M	Ueber den Tumor des Zirkelhirns. Wochenschr. 1891, 43, 104-111

right superior quadrigeminal body. The posterior commissure was intact, the habenular commissure was torn in its central part, all veins of Galen were intact.

The tumor was firm, slightly knobby, smooth surfaced, grayish yellow mass by 5 by 16 millimeters in diameter, to which were adherent on its upper and posterior surface few elongated shreds of tela choroides which extended to embed themselves in the body of the growth on its posterior-inferior flattened ragged surface, after stretching over three-quarters of the tumor's circumference. The surface shown by sections of the Zenker-fixed specimen was firm, and exhibited numerous minute cysts scattered but irregularly about, varying from pinpoint size to 5 millimeters in diameter. Between varied considerably macroscopic calcification was not found. Macroscopic examination showed remarkable array of tumor (Fig. 7) many of the cysts were lined with stratified epithelium, each overlying definite columnar, beneath these were sweat glands, sebaceous glands, areolar, elastic, and connective tissue, intermingled with smooth muscle. No hair follicles or hair was found, other small cysts were lined with cuboidal epi-

thelium, and some with cuboid epithelium, definite bronchial sacs and small bronchial tubes were found, the surrounding tissue here being composed of areolar adipose, and connective tissue intermingled with processes of cartilage of non-branched strands of striated muscle, and strands of cartilage scattered formations of cartilage in all stages of development. are found throughout the tumor together with occasional islands of osseous tissue, but no cortical bone or marrow was found. Few collections of calcification were present, no areas bearing resemblance to osseous enamel organ were found. Choroidal plexus tufts, a good blood supply had been carried deeply into nearly closed small cavity on the posterior surface of the tumor. Gliar tissue was not uncommon both in the periphery and within the body of the tumor, but no typical substance was found, occasional nests of ganglion cells and bare non-membranous fibers were present in relation to the periphery of gliar areas. Within the zones of tumor not only were pseudo-rosettes often found, and fully differentiated ependymal lining to at least one small cyst, but multiple ependymal tubularization was occasionally present within the gliar network, as is found in congenital or traumatic tumors of the aspect. Vascularization was not abundant, but no areas of necrosis were present.

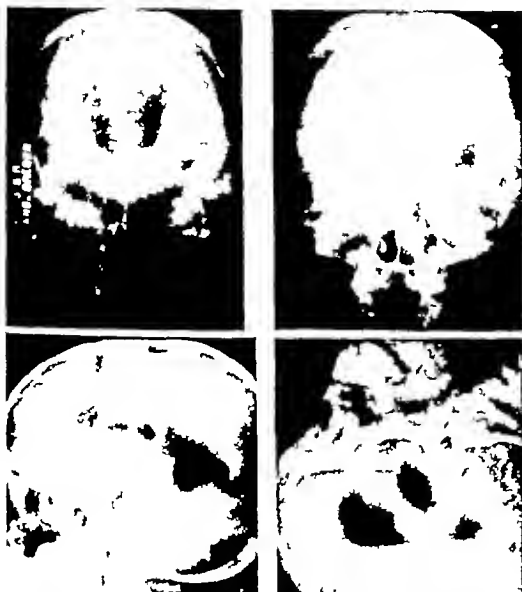


Fig 1 Ventriculograms a An anteroposterior projection showing uniform symmetrical hydrocephalus of lateral and third ventricles b, A postero-anterior projection showing undisplaced lateral ventricles with hydrocephalic third ventricle containing a rounded mass posteriorly projecting into it from above c, One film of a lateral stereoradiogram showing convolitional atrophy with hydrocephalic dilatation of lateral ventricles and of foramina of Munro, the anterior part of the third ventricles is faintly demonstrated. d, A view showing filling defect in postero-superior portion of third ventricle; air is in both frontal and temporal ventricular horns and in third ventricle

This teratoma has a more complicated structure than any other described in literature available to me, structures derived from all three germ layers are indubitably present. If a teratoma (as distinguished from a dermoid) be a tumor comprised of tissue arising from more than one germinal layer, many recorded pineal teratomas are entitled to their designation only by virtue of small islands of cartilage or of smooth muscle within or about a tumor composed predominantly of true pineal parenchyma in some stage of differentiation<sup>1</sup> (13), while others described in the literature as "dermoid" (e.g., 2<sup>2</sup>) actually contain at least epidermal and mesenchymal structures, and should be denominated teratoma. The problem of identification, however, is not so uncomplicated as would at first appear, for connective tissue is present in pineal trabeculae, the gland is invested with pia, has a neural pedicle, and, at least

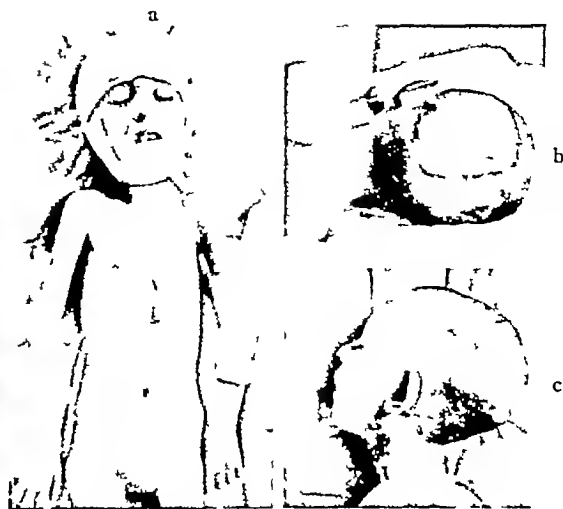


Fig 2 Patient 2 days before third stage operation a shows emaciation and normal genital development. b and c are views of the occipital wound after two interventions

in certain vertebrates (calf, ox), smooth muscle and striated muscle (24) are normally present, human pineal tumors containing fibers of striated muscle in their capsules have been excluded on occasion from teratoma classification by some authors (26). In gliomas, Bailey and Cushing recognized the logic of accepting the predominant type of tissue present as indicative of tumor name and tumor behavior, if such a practical rule were adopted for reported pineal teratomas, several could be excluded from Table II.

It is probable furthermore that not all tumors reported as pineal teratomas actually arise from the pineal body itself. It is true that teratomas may actually arise from within pineal substance, and that pineal tissue is then found embedded in the walls of the tumor (2), but Ewing (8) mentions that in cases of "pineal teratoma" a normal uninvolved pineal body is sometimes found, moreover, in the case under report a flattened pineal body of normal structure for the patient's age was found pressed backward and downward onto the right anterior quadrigeminal body and free underneath the tumor itself. Teratomas, of course, may occur elsewhere within the cranial cavity than in the region of the pineal (parahypophyseal, occipital, etc.) and dermoids—often containing ciliated epithelium (17)—are not uncommon throughout the midline craniospinal axis, but one enters an exceedingly fascinating field in tracking down possible origins for what may be termed para-pineal teratomas, such as the one herewith considered.

<sup>1</sup> Such tumors as these might strictly be denominated teratoids

<sup>2</sup> Contained corium, squamous epithelium, hair, cholesterol, sebaceous glands, adipose tissue, cartilage, lamellar bone, marrow, osteoid tissue, etc.

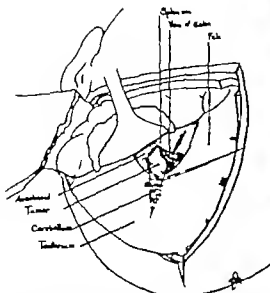


Fig. 3. Operative field, drawing elaborated from immediate postoperative sketch. The exposure might be further facilitated by moving up and the inferior border of the falx, but the additional mobility thus given the great vein of Galen augments its chances of fatal rupture during removal of the tumor.

#### POSSIBLE ORIGINS

A not uncommon origin for complex tumors is from embryonic estiges. The human third ventricle cavity is remarkable embryologically for the numerous outpouchings to which it gives rise and which ultimately come to form special organs—pulchum, optic vesicles, infundibulum, post infundibula recess (28) choroid plexus, paraphysis, pineal, and subcommissural organ (5). In addition, there occur in embryonic life a parapineal process and two precommissural organs. To quote from Wilder (34)



Fig. 4. Photograph of the Zerkow fixed parapineal teratoma removed at operation.



Fig. 5. Above, Median sagittal section of brain showing left half of tumor bed. Below, The conditions at the operative field and the corresponding back of regional trauma possible with the Brownie operation procedure, not the intact posterior commissure and the ruptured subarachnoid space.



Fig. 6. Photomicrograph demonstrating normal paraneuronal histology in the somewhat flattened prefrontal body found pinned down and and to the right by the overlying parapineal teratoma.

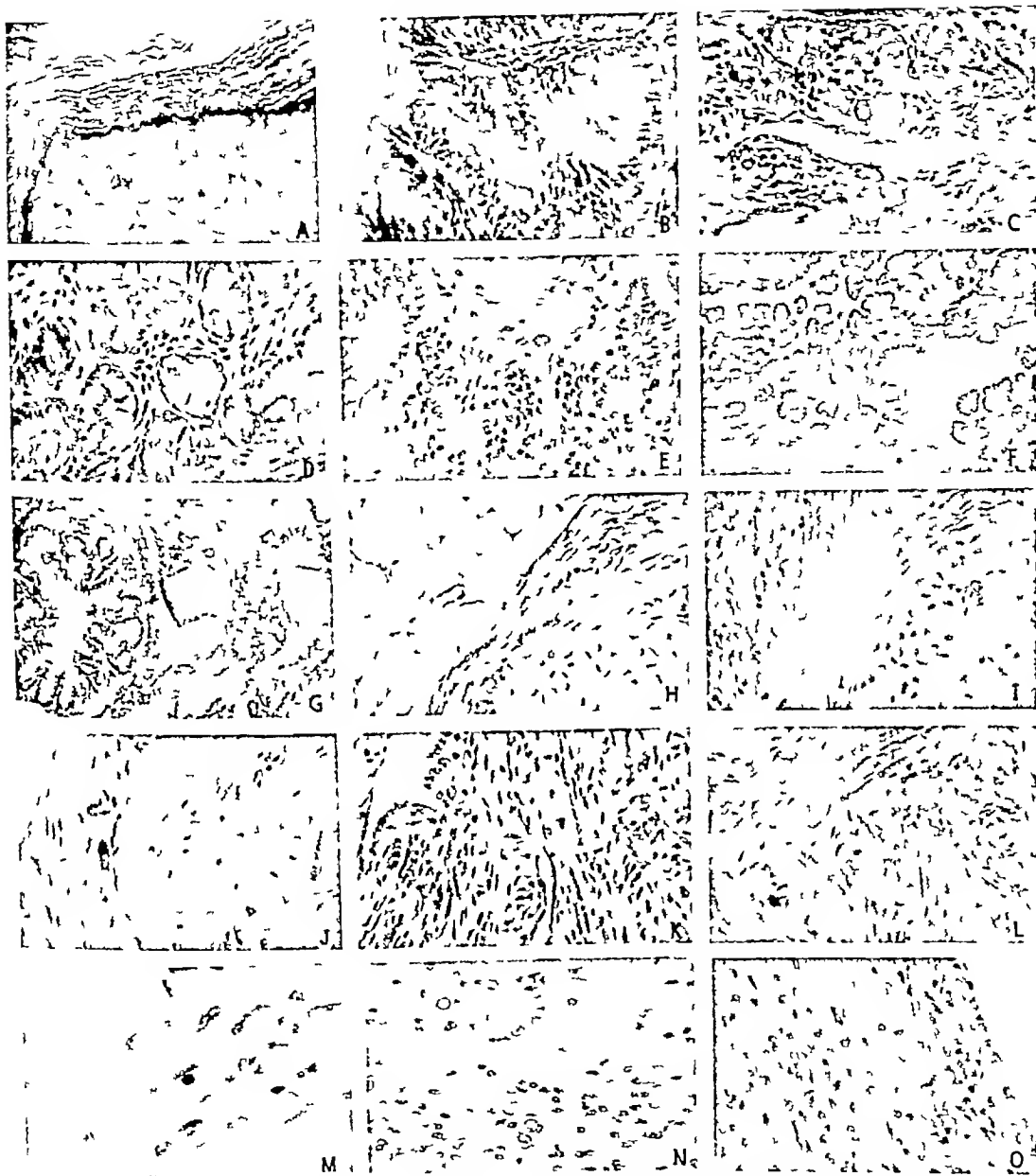


Fig 7 Photomicrographs showing the variety of tissue comprising the teratoma a, Corium and cornified layer of squamous epithelium b ciliated epithelium, c nest of ganglion cells at edge of glial island—a blood vessel is in the lower left field d sebaceous glands, e ependymal tubulization of marginal glia f choroid plexus g small bronchus with cartilage islands, and areolar tissue, h, adipose and

connective tissue with segment of island of cartilage, i calcospherite in cartilage, j osteoid tissue, k smooth and striated muscle near bronchiole, l interlacing striated muscle—note abundance of cross striations, m, oil immersion of cross striations shown best in oblique fiber near top of field, n astrocytic feltwork in body of tumor o adult ependymal lining of microcyst



Several of these (outpocketings) occur along the dorsal aspect, where in addition to the choroid plexus of the third ventricle, there appear in the thin roof typically three median diverticula, which, owing to the varying grades of development, which they show in different animals, have been more or less confounded with each other. The most anterior of these is the paraphysis. Posterior to the

chiasm trunks cross there are two possible diverticula in the diencephalic roof, both correctly termed epiphyses, parietal organs, or parietal organs. Both show a tendency to pass through the skull and into position directly beneath the skin in the middle line, developing there rudimentary sense organs of uncertain nature but probably an eye in each case. The identity of the structure may always be determined from its central connections.

In the cyclostomes, fishes, and reptiles both epiphyses are usually present and one or the other may attain a high degree of development, in some cases reaching its height during embryonic life, and in others appearing as a well formed organ in the adult. Thus in the cyclostome *P. trutta* the optical nature is indicated by the presence of pigment in what may be ventral retina. In the teleosts, the epiphysis passes through a foramen foramen in the skull and reaches the surface, where its terminal organ is visible. The highest development is reached among certain birds (e.g. *Halimastur procerus*) where the terminal organ lies in a socket, the parietal foramen, formed in the interparietal suture, and represents a fairly good eye. Its pigmented retina, more or less stalked, and well developed, connects the terminal organ with the brain. Above this on the surface, is situated a transparent scale surrounded by a ring of smaller opaque ones, making conspicuous object on the head of these forms. In birds and mammals the epiphysis is reduced to the form of the so-called pineal gland, pushed backward from its original position (and deeper) by the growth of the parts.

In human development almost all of these diverticula, which sometimes indeed become racemose, are lined with some variety of cuboid or columnar epithelium analogous to ependyma, and may at times attain cilia upon their free surfaces (32) reported tumors of the adult human paraphysis are remarkable for their simple histological structure (27-31) complexity of structure in such third ventricular diverticula is encountered developmentally only when apposition to ectoderm is again attained (eye, hypophysis parietal eye). Alexander has described a mid habennular nodule in 5 per cent of human embryos ( ) corresponding to the mammalian corpusculum parietale (Krabbe), a possible vestige of the more anterior epiphysial diverticulum first described in human beings, I believe by Mikulovics ( 877) I am unable to ascertain definitely whether the tumor

under report arose from one of the lateral paired precommissural organs (32) or from the mid habennular corpusculum parietale, but, from macroscopic examination, incline to the latter view. The internal histological structure of the corpusculum is unknown to me. The comparative and human embryology (and histology) of the pineal body itself affords no reliable clue for the development of teratomas. A continuing uncomplicated proliferation of any of the four vestigial structures of this region (corpusculum, pineal, precommissural organs) is therefore insufficient to explain a trigeminal layered tumor.

However since most of the diencephalic roof structures are midline, or immediately about it, Cohnheim's inclusional theory might operate here with peculiar force and, through the enfolding of epithelial vestiges, could explain not only the regional dermoids, lipomas, cholesteratomas, and colloid mucinous cysts, but also by more primitive inclusion of totipotent blastomeres, even account for the occurrence of teratoids and teratomas. The stimulus to proliferation would be under this theory somewhat more obvious here as a continuing process than in the often delayed development of most other parenchymal neoplasms—for indeed 75 per cent of pineal teratomas are found to occur in pre-adolescents (Table II) their crucial relation to the tentorial incisure causing them early to become manifest.

Another possibility remains to be considered that of parodogenetation of a fertilized fusal polar body. Askanazy indeed has even reported a primary chorio-epithelioma of the pineal body. This possibility might have had peculiarly effective force until 1921 for until that year all reported teratomas had been found solely in males. Luce, however at that time reported an undoubted pineal teratoma which had occurred in a 5½ year old girl ( 8) Of course to confirm Mendel's male sex linked character pineal teratomas could have been demonstrated as occurring in alternate generations of males, transmitted through unaffected females such demonstration has not been brought forward. Ferguson, however has recently demonstrated presence of prolan A in the urine of males (9) with teratoma testes whether

See Dandy A. On the structure, development, and morphological interpretations of the parietal organs and adjacent parts of the brain in the Teleosts (Sphæromastacaceans). J. Roy. Soc. Lond. 1909, June.

These statements are based principally on the work of Mikulovics (14), Alexander (15), and Krabbe (16) being mainly on sections of the pineal body of diverticula which arise from the dorsal outpocketing of the third ventricle of some glandular fish. They are described by Alexander (16) as nearly resembling the brain stem and from descriptions of many of the rudimentary human precommissural organs are the homologues of these structures.

The term pineal is applied to such an outpocketing projecting from the brain stem and containing a mass of cells (17).

Parthenogenesis development of an unfertilized isolated polar body would come within scope of this category as well.

If pineal teratomas were based on such solitary sex cells, one might expect many parthenogenetic observations of chromosome number in the isolated polar body (female chromosomes) would regularly be the normal diploid number.

Female sex in chorio-epithelioma of either sex and of common origin, pregnancy, the absence of prolan A in cases of teratomas born with adult testis, tumours (chordoma) frequently on chorio, etc. are found in its work less than in cases of compound of pure embryonic origin, principally therefore that even if prolan A had been present before the moment single have been undetectably small.

this be a reaction common to all teratomas is yet unknown. Moreover, Silberstein and Engel believe that they have demonstrated an estrogenic substance in the normal beef pineal body. In the present case no tests for prolan were made, illuminating though they might have been, indeed I was delighted to confirm operatively a clinical diagnosis of tumor of pineal region, let alone to attempt polishing the diagnosis by prediction of the precise histological characteristics of the neoplasm.

Since there is no conceivable possibility of semen coming in contact with the pineal or with primitive inclusional ova dormant there, it is not necessary to consider non-coetaneous generation, as one inevitably must in ovarian or testicular teratomas.

## SUMMARY

A case of parapineal teratoma is recorded, this is the first removed operatively, the operation was not clinically successful. Operative procedures, tumor classification, and possible origins of the tumor are considered.

Grateful acknowledgment of criticism and aid is made to Drs. Charles Manlove, Albert Mathieu, Harry Blosser, Matthew Riddle, Louise Eisenhardt, and George Snyder, Miss Wanda Templeton assisted in the histologic work.

## BIBLIOGRAPHY

- ALEXANDER, A. Zur Frage der Existenz eines Parietalorganrudimentes. *Arch. d. neurol. Inst. a. d. Wien Univ.* 1932 34 252-265.
- ALTMAN, F. Ueber ein Dermoid der Zirbeldrüse. *Wien klin. Wchnschr.* 1930 43 108-111.
- ASKANAZY, M. Teratom und Chorioepitheliom der Zirbel. *Centralbl. f. allg. Path. u. path. Anat.* 1900 17 872.
- BAILEY, P. and CUSHING, H. A Classification of the Tumors of the Glioma Group on a Histogenetic Basis with a Correlated Study of Prognosis. Philadelphia J. B. Lippincott 1926.
- CUSHING, H. *Intracranial Tumors*. Springfield Ill. C. C. Thomas, 1932.
- DANBY, W. I. An operation for the removal of pineal tumors. *Surg. Gynec. & Obst.* 1911 33 115-119.
- FRANKEL, I. Vorl. ueber den Bau der nervösen Zentralorgane des Menschen und der Tiere. 2th ed. 2 vols. Leipzig I. C. W. Vogel 1904.
- LIVING, J. *Neoplastic Diseases. A Treatise on Tumors*. 3d ed. Philadelphia W. B. Saunders Co. 1918.
- LITTLESON, K. S. Quantitative behavior of prolan A in teratomata testis. *Am. J. Cancer* 1934 18 69-95.
- LORESTER, O. Incephalographische Erfahrungen. *Ztschr. f. d. ges. Neurol. u. Psychiat.* 1914 64 51-584.
- LUTON, J. I. and BAILEY, I. Tumor in the region of the third ventricle: their diagnosis and location to pathological sleep. *J. Nerv. & Ment. Dis.* 1919 60 1-25 145-164 261-277.
- HARRIS, W. and CAIRNS, H. Diagnosis and treatment of pineal tumors with report of a case. *Lancet* 1932, 1 3-8.
- HORRAN, G. and BAILEY, P. Pineal pathology further studies. *Arch. Neurol. & Psychiat.* 1928, 19 304-413.
- KRABBE, K. H. Histologische und embryologische Untersuchungen ueber die Zirbeldrüse des Menschen. *Anat. Hefte* 1916 54 101.
- Idem. *L'Organe sous-commissural du cerveau*. *Presse méd.* 1933 41 1750-1752.
- KRAUSE, F. Operative Freilegung der Vierhügel nebst Beobachtungen ueber Hirndruck und Dekompression. *Zentralbl. f. Chir.* 1920, 53 2812-2810.
- KUBIE, L. S. and FELTON, J. F. A clinical and pathological study of two teratomatous cysts of the spinal cord containing mucus and ciliated cells. *Surg. Gynec. & Obst.* 1928 47 297-311.
- LUCE, H. Zur Diagnostik der Zirbelgeschwulste und zur Kritik der cerebralen Adipositas. *Deutsche Ztschr. f. Nervenhe.* 1921 65 137-210.
- MARBURG, O. Zur Kenntnis der normalen und pathologischen Histologie der Zirbeldrüse. *Arch. d. neurol. Inst. a. d. Wien Univ.* 1908 17 217.
- McLEAN, A. J. *Handb. d. Neurol.* 2 Aufl. Bd. XIV. Berlin J. Springer 1935 (in press).
- MIHALKOVICS, V. Entwicklungsgeschichte des Gehirns nach Untersuchungen an höheren Wirbeltieren und dem Menschen. Leipzig W. Engelmann 1877.
- NAFFZIGER, H. C. Brain surgery with special reference to exposure of the brain stem. *Surg. Gynec. & Obst.* 1928 46 241-248.
- NASSETTI, F. Dell' operabilità delle vie di accesso ai tumori della ghiandola pineale. *Policlin. sez. chir.* 1913 20 407.
- NICOLAS, A. Note sur la présence des fibres musculaires striées dans gland pineale de quelques mammifères. *Comp. rend. Soc. de Biol.* 1900 72 873-877.
- OPPENHEIM, H. and KRAUSE, F. Operative Erfolge bei Geschwulsten der Sehhügel und Vierhügel. *gend. Berl. klin. Wchnschr.* 1913 50 2316-2322.
- PAPPENHEIM, A. M. Ueber Geschwulste des Corpus pineale. *Arch. f. path. Anat.* 1910 200 12-141.
- PENFIELD, W. Diencephalic autonomic epilepsy. *Arch. Neurol. & Psychiat.* 1929 22 358-74.
- RICHTER, C. P. and BENJAMIN, J. A. The third ventricle: conformation of the floor and its relation to the meninges. *Arch. Neurol. & Psychiat.* 1914 31 1076-1037.
- KORSCHACHT, H. Zur Pathologie und Operabilität der Tumoren der Zirbeldrüse. *Beitr. z. klin. Chir.* 1913 8, 451-474.
- SILBERSTEIN, F. and FENDEL, P. Ueber das Vorkommen einer oestrogenen Substanz in der Hypophyse. *Klin. Wchnschr.* 1913 46 908-910.
- TANDLER, J. and KANZI, E. *Chirurgische Anatomie und Operativtechnik des Zentralnervensystems*. Berlin J. Springer 1929.
- TURKAWITZ, N. Entwicklung des Zwischenhirns beim Menschen. *Organ u. Entwicklungsgeschichte Anat. Anz.* 1913 47 3-25.
- WATSON, W. P. A surgical approach to the removal of certain pineal tumors. *ref. of a case Surg. Gynec. & Obst.* 1931, 5 716-720.
- WILDER, H. H. *The History of the Human Eye*. 3d ed. New York H. H. & C. 1917.

a case which had resisted two attempts at repair in a conventional manner seemed quite striking. It is obviously best adapted to cases in which there is no true evulsion or destruction of sphincters, but merely its loss of function through having been stretched or markedly attenuated.

## BIBLIOGRAPHY

- BOY, EY. V. Diurnal incontinence of urine in women. *J Obst & Gynec* 9 3, 70 118
- DEAN, C. L. Transplantation of gracilis muscle for incontinence of urine. *J Am M Ass* 9 6, 86 8
- DOUGLAS, D. Urinary incontinence in women, with special reference to the operative treatment in young multiparae. *J Obst & Gynec* 9 14 31 46
- FRIED, H. D. Urinary incontinence in women. *Surg Clin America* 9 2, 4 240
- KELLY, HOWARD V., and DUNN, WILLIAM M. Urinary incontinence in women—about residual injury to the bladder, report of cases. *Surg Gynec & Obst* 9 14, 18 444
- MCGARY, J. A. Reconstruction of urethra. *Am J Obst & Gynec* 9 1, 34 362
- THORP, F. J. A new operation for urinary incontinence in women by transposing levator an. muscles. *Am J Obst & Gynec* 9 8, 77 221
- DEAN, R. F. The use of the cystoscope as control in the diagnosis and treatment of cystocele. *Urol & Cutan Rev* 9 12, 36 87
- WARD, G. C. Reconstruction of the urethra after complete loss complicating an ectopic ecto-vaginal fistula. *Surg Gynec & Obst* 9 12, 17 678
- WYLLIE, B. P. Imperfect urinary control following childbirth and its surgical treatment. *Brit M J* 9 14, 366
- WILLIAMSON, J. THORP. ALL. Diurnal incontinence in women. *Arch Surg* 9 14, 28 348
- YORST, E. L. Urinary incontinence in the female. *J Am M Ass* 9 2, 70 753
- YORST, H. H. Operation for the cure of urinary incontinence. *Surg Gynec & Obst* 1919, 28 24

THE SIGNIFICANCE OF BLEEDING OR DISCHARGE FROM THE NIPPLE<sup>1</sup>

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EDUCATIONAL propaganda for the prevention of cancer is responsible for more women seeking surgical advice than ever before. Bleeding or a discharge from the nipple is not infrequently one of the symptoms that causes an anxiety on the part of a patient. This symptom is recognized by surgeons and pathologists as indicative of pathology in the mammary gland but unfortunately its significance, as well as its bearing on treatment, causes conflicting opinions.

Topic states that, in a few cases, loss of blood from the nipple results from benign intracanalicular papillomatous growths but most frequently the blood results from an endocanalicular ductal carcinoma. Adair is of the opinion that a dark, bloody discharge always is indicative of a ductal carcinoma. Deaver and McFarland interpret blood from the nipple as being attributable in the majority of cases to papillary growths or to benign intracanalicular papillomas. Lewis believes a serohemorrhagic or brownish discharge is not a clue to malignancy but is associated with intracanalicular papillary cystadenoma and the adenocystic type of chronic mastitis. Saar considers that there is no relationship between a bleeding from the nipple and carcinoma. Greenough and Simmons report 20 cases of cystadenoma, in 11 of which there was a discharge from the nipple and 3 of these were found to be malignant. Rodman regards cystadenomas situated immediately behind the nipple with a discharge of blood in patients 48 to 49 years of age as being potentially malignant from their inception. Bloodgood found that less than 1 per cent of his cases of carcinoma of the breast had bleeding from the nipple. His practice is to remove every palpable tumor in the breast regardless of the discharge from the nipple and to make a diagnosis of the tumor by immediate frozen section at operation. His studies reveal that a patient with a lump in the breast and a discharge from the nipple which has not been noticed longer than a month has an 80 per cent chance of having a benign lesion. Following a recent review of his cases with discharge from the nipple that have not been operated, he feels convinced that these patients run no more risk of developing cancer than does a woman with no discharge (a).

Cheatle and Cutler, in their recent book, *Tumors of the Breast* differ in opinion with Blood-

good. They discard the old nomenclature of chronic mastitis and chronic cystic mastitis and offer an entirely different and new classification. This is based upon conditions noted in the breasts as mastitis which are more physiological than pathological, and those noted with cysts and papillomas that are distinctly pathological. The physiological type of breast they call mastoplasia, the condition being found in some form in all breasts up to the menopause. The early pathological state of the breast they term cystiphorous desquamative epithelial hyperplasia, which in the literature in the past has been known as senile parenchymatous hypertrophy (Bloodgood), Schimmelbusch's disease, Reclus disease, and chronic cystic mastitis. This condition begins in the later 20 years of life and there is found either a small cyst or numerous small and large cysts. As the cysts become older, during the late 30 or 40 years of life, there can occur certain neoplastic changes without any clinical indications or symptoms noticed by the patient. Possibly the first unusual symptom occurring in this stage is a discharge of serum or blood from the nipple with the appearance of an increase in pain. This would be indicative of a single or multiple benign papilloma or a carcinoma. The supervention of the neoplastic change is not a necessary consequence, and the cystic condition may remain in the pure state. These authors state that a carcinoma may arise in the apparently single cystic lesion, in the generalized multicystic state, and in those localized to a single duct, its branches, or acini. Malignancy appears about 25 to 30 years after the incidence of the cystiphorous stage and develops in small cysts in 20 per cent of all cases of carcinoma of the breasts. They further state that a carcinoma may originate in the ducts of the nipple which presents characteristic findings of a small, not very malignant tumor, giving a spontaneous discharge of blood from the nipple with early ulceration. This tumor most often arises from the duct epithelium and, according to Muri, is the cause of Paget's disease. When the tumor is immediately beneath the nipple, there may be an early fixation and retraction of the nipple and blood may be the very first symptom.

A discharge from the nipple may occur in the newborn. It is of a milky character and is associated with bilateral hypertrophy of the breasts.

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# LOSS OF URINARY CONTROL ASSOCIATED WITH RELAXATION OF THE VESICAL NECK

## A MODIFIED TECHNIQUE FOR ITS TREATMENT

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**I**NCONTINENCE of urine is frequently associated with the trauma of childbirth or some sort of dystocia. The degree of the patient's difficulty ranges from the loss of small amounts of urine upon coughing or sneezing to complete incontinence with constant soaking of the patient's clothing with urine. This is often but not always associated with cystocele and relaxation of the urethral floor. Cystoscopic examination usually reveals a symmetrical deformity of the sphincter at the vesical neck showing a defect at the posterior or vaginal side of the sphincter (8). Operative treatment alone is of any avail.

A large number of methods have been proposed for the treatment of urinary incontinence of this type (1, 3, 10, 11, 1) and have been employed with varying success. The Kelly method has been the most successful procedure in this type of incontinence and is usually sufficient to cure the average case of relaxation of the vesical neck. The anatomical and functional relationship of the internal and external sphincters and the importance of the fascial support have been very adequately discussed in the papers of E. L. Young, Bonney Watson, and others. There are, however, certain cases with marked thinning of the bladder wall at the vesical neck, the site of the internal and external sphincters (usually indistinguishable from one another at operation) in which it is very difficult to implicate the relaxed tissues of the redundant vesical neck sufficiently (about a Pezzer catheter) to insure the competency of the sphincter. The difficulty lies in the fact that only very small superficial sutures may be taken in placing the mattress sutures employed in the Kelly technique and unless extreme care is employed, there is danger of penetrating the vesical mucosa, with the subsequent danger of the development of a fistula, a most troublesome and embarrassing accident.

These considerations have resulted in several failures of complete functional cure following the Kelly technique, presumably due to the fact that the plicating stitches were placed too superficially and thus in turn due to the fact that there seemed to be no muscular or fascial structure worthy of the name to suture adjacent to neck of the bladder. The plan suggested itself whereby the tissues

surrounding the vesical neck might be thickened sufficiently to permit the plicating sutures to be passed more boldly and deeply, imbricating more tissue. This was effected by the employment of superimposed plicating sutures originally employed, by Gersuny and Saenger to reduce the bladder wall in large attenuated cystoceles. The prime purpose of this procedure however is to insert a valve like bunching of tissue at the lower margin of the vesical neck.

This method was devised after two unsuccessful attempts to cure a case of relatively simple post partum incontinence. This patient was seen first on November 23, 1933.

She is a primipara, white, aged 24 years, who had been subjected to a complicated breech extraction procedure 6 months previously and since then had had complete chronic urinary incontinence.

On examination the neck was found to be moderately relaxed. The anal sphincter was in good condition. The cervix showed laceration with moderate erosion. There was a fairly large cystocele the bladder coming down low on the cervix. There was rather marked pooling under the urethral orifice but this was proved by sound not to be the urethra. The fundus was in retroversion, readily movable. It is normal in size and consistency.

**Operation.** A median longitudinal incision was made, the bladder mobilized and adnexed. A Pezzer catheter was placed in the bladder and Kelly mattress sutures were placed plicating the neck of the bladder anterior to the "drag" of Pezzer catheter. Each was withdrawn before the sutures were tied. This narrowed the vesical neck rather markedly. Anterior colporrhaphy, as done, the fascia being sutured in separate layer. The urethra was mobilized and advancement of the urethra was performed after the manner of Park, horizontal denudation being made above and lateral to the urethral orifice. The defect was closed with interrupted chromic catgut sutures. The vesical mucosa was sutured with interrupted sutures of chromic catgut N. The patient was catheterized frequently and her urinary control, as much improved but as not complete even during her stay in bed. On discharge from the hospital her control was further improved but there was still considerable nocturnal leakage unless she emptied her bladder very frequently.

The patient was discharged with the result and was next operated upon April 7, 1934. On examination there was evidence of cystocele repair well healed. The urethral orifice was rather dilated and seemed large on passage of sound. The uterus, as in preparation and was freely movable. There were no lateral masses. The patient had dorsal urinary incontinence only. Generally she retained her urine perfectly at night if she got up to void once or twice.

**Second operation.** A Pezzer catheter was placed in the bladder and the vesical neck was demonstrated as usual.



Fig 1 Diagrammatic view of pursestring *in situ* showing sutures placed in the vesical neck.

high level. The urethra was dissected out and Kelly mattress sutures of chromic catgut No. 1 were placed in the musculature above and below and deeply into the fascia overlying it. The urethra was covered further by two interrupted sutures narrowing it anteriorly toward the urethral orifice. Several interrupted sutures were placed in the fascia posterior to the vesical neck, giving the bladder and presumably the sphincter mechanism additional support. The mucous membrane and fascia were closed in one layer with interrupted sutures of catgut No. 1. This material was used in very small round needles throughout. Patient was catheterized every 6 hours and a retention catheter was not employed at any time. The patient was kept in bed for 2 weeks and was discharged from the hospital with her condition essentially unchanged. Her urinary control was improved, but there was slight and constant leakage. After her return home, her condition failed to improve. Unfortunately, it is unusual for urinary control to improve after discharge from the hospital. More frequently, at a later date, incontinence may recur following an apparently successful operation. In view of the disappointing result it seemed advisable to attempt something else in an effort to restore the competency of the vesical sphincter mechanism. It was decided to attempt to produce a valve or obstruction at the vesical neck.

**Third operation.** A median incision was made through rather dense scar tissue overlying the bladder and the mucosa was carefully mobilized, leaving a rather thin fascial investment covering the vesical musculature.

Two superimposed pursestring sutures approximately 2 centimeters in diameter were placed just anterior to the vesical neck as demonstrated by the "pull" of a Pezzer catheter. The first suture was invaginated and tied (Fig 1), after the manner of Gersuny and Saenger, and a second pursestring suture was then placed immediately over the first suture and likewise invaginated. This narrowed the bladder from side to side considerably. Two Kelly mattress sutures were placed immediately over the superimposed purse-



Fig 2 Above Sagittal section showing position of pursestring and Kelly mattress sutures. Below, Sutures tied showing invagination of thinned out vesical neck.

string sutures (Fig 2). The Pezzer catheter was withdrawn, being carefully stretched over a stylet before the mattress sutures were tied. Patient was returned to the ward and was catheterized every 6 hours for 48 hours.

She started voiding spontaneously after this time and was entirely continent from the date of operation. She had not the slightest leakage at any time in bed. She was completely continent when she got up on her fourteenth hospital day. She, however, had slight leakage upon coughing. Cases of an attenuation or atrophy of the musculature structures surrounding the vesical neck may be susceptible of attack by this rather simple device. It suggests the production of something analogous to a median bar in the prostate represented diagrammatically in Figure 2.

We have not had the opportunity of inspecting the vesical neck since the operation but cystoscopy will be done 3 months after operation. It is dangerous to subject a recently repaired sphincter mechanism to the dilatation incident to cystoscopy. It is quite possible that the invaginated tissue inside the pursestring sutures may atrophy and control subsequently may not be so complete as at present. However, at the present time, 2 months after operation, the "plug" mechanism, collapsing the urethra from below at the vesical neck, is functioning well.

The success of this simple procedure restoring competency of the vesical sphincter mechanism in



Fig. Dilated duct with retained secretions. Periductal round cell infiltration. Dilatation of ducts was noted in both peripheral and terminal ducts.



Fig. Dilated duct with areas of single layer epithelium showing several layers thick. A papilloma is found in anastomosing sections.

It very shortly disappears by cleansing the nipple and the application of protective dressings. It may be complicated by infections, abscesses, or erysipelas with ultimate death.

In adults, a discharge from the nipple may be serous, thick greenish, whitish or of a bloody character.

A serous discharge is usually unilateral and may occur with infection of the ducts of the nipple. Its presence should be a cause of anxiety particularly when a tumor is discovered in the same breast as such a discharge often accompanies malignancy. A patient with this type of discharge and no other malignant findings should remain under constant observation until the diagnosis of malignancy can be definitely eliminated.

A discharge of a thick, greenish material from the nipple occurs in young married women who have borne children. It usually is bilateral, is not spontaneous, and is caused by the retention of secretions in dilated ducts following lactation.

A whitish discharge simulating milk is associated with the more or less rare tumor galactocoele. This is painless, circumscribed fluctuating doughy tumor occurring with lactation which can-

not be very easily confused with any other pathological condition in the breast. The discharge may be white due to pus, or in rare cases, to masses of desquamated epithelial cells.

Discharge of blood from the nipple may be traumatic, is easily recognized by the history and on examination there is evidence of ecchymosis. In determining the extent of the injury to the breast, assistance may be possibly obtained by transillumination. Should a hematoma be present such an examination reveals a characteristic opacity irregular in outline more dense in areas than in others with very irregular edges which gradually fade at their margins. These findings may persist for as long a period as months. By comparison the shadow cast by carcinoma is usually much lighter fairly homogeneous, with more regularity of its edges. If cancer is suspected further investigation should be made.

Papillomas are probably the most frequent causes of bleeding from the nipple occurring usually in the late 30 or early 40 years of life. The principal etiological factor in the development of papillomas is conceded to be some form of irritation either stagnation of the contents of ducts following lactation, stagnation of desquamated epithelial cells, micro-organisms, or possibly trauma. Papillomas of the breast can disappear as any wart, and spontaneous cures have been



Fig 3 Dilated duct to left is filled with blood. Dilated duct to right shows broad base, sclerotic papilloma

reported. It is very doubtful however if the papillomas actually disappear. It is more likely they become quiescent with an absence of discharge of blood from the nipple and all other symptoms until possibly years later when symptoms again begin to appear.

Another breast lesion producing a discharge of blood from the nipple is Bloodgood's "Varicocoe Tumor of the Breast." This mass is found to be single, multiple or to be present with other pathological conditions. Patients having this condition are at the menopause or have passed it. The tumor is characterized by a doughy and worm-like feeling, is painful and tender. The discharge from the nipple is grumous, brownish material, varying in color. When this condition can be recognized clinically, an operation is not indicated.

The early recognition of Paget's disease and the radical removal of the affected breast affords greater success in the treatment of this condition. Although the pathological process of Paget's disease is slow, seldom infiltrates and rarely metastasizes, a carcinoma very frequently exists in the underlying breast without any of its usual clinical symptoms or findings. Hertzler has found that cancer of the breast follows the onset of Paget's disease within 2 years and usually within 1 year.



Fig 4 Dilatation of ducts and epithelial hyperplasia of ducts but no extension beyond normal confines. The epithelial hyperplasia and hyperchromatism bespeak early malignancy.

A thin, clear, serous straw colored fluid occurs only in the cystic forms of sarcoma. According to Gross, it is present in 10 per cent of the cases of sarcoma. The large size of the tumor, its circumscription, mobility, lobulation, elasticity, and the history of its rapid growth serve to differentiate it from carcinoma and, as a rule, from pure adenofibroma. In this pathological condition there is no metastasis to glands, no adherence to the skin, and no retraction of the nipple.

A spontaneous and intermittent discharge of blood similar to that seen with a papilloma may be produced by a duct carcinoma or a carcinoma that arises from terminal ducts and acini combined. The discharge may occur at intervals of weeks, months, or years and its character is no indication of the type of the disease present, malignant or benign. Pain is always present in these pathological conditions, varying in extent from a mere discomfort in the breast to the severe pain of distended ducts.

The diagnosis in the early stages of both benign and malignant conditions is often hindered by the absence of a demonstrable tumor. In a case of





Fig 5 Large compound papilloma which was found in dilated duct. It measured about five tenths centimeter in diameter. There was no evidence of malignancy.



Fig 6 Large compound papilloma extending into dilated duct with sclerosis of portion of papilloma. There is no evidence of malignancy.

bleeding from the nipple with no palpable tumor present in the breast, the roentgenographic findings being negative, one can conclude that a papilloma is present in one of the ducts. The exact location of a papilloma can frequently be determined by locating a tender point and exerting pressure on it, when blood is expressed from the nipple. When the papilloma is palpable it appears to be very elastic, elongated, is freely movable and lacks the hardness of a carcinoma.

The variance of opinion regarding the significance of bleeding or discharge from the nipple and its bearing on treatment lead to a review of the records of all patients with breast conditions that had been treated at Research Hospital the past several years. Our study revealed only 6 cases that had at some time during their clinical course noticed bleeding or discharge from the nipple. These patients were operated upon by various members of the staff and the specimens removed at operation were examined and reported upon by the hospital pathologist, Dr F C NARR.

**CASE** Hospital N #3474 Mrs V W aged 44 years, 3 pregnancies. Discharge had been noticed from the right nipple for weeks, the discharge first resembling milk, later becoming blood tinged. The nipple as sore and under it the patient could feel small mass which was not tender. A simple amputation of the breast was done. Pathological examination revealed all of the ducts to be markedly dilated and filled with light green, soft, potty-

like matter. About them there was loosened connective tissue proliferation but no cyst cavities. Sections showed great distention of peripheral and terminal ducts with retained secretions but no neoplasia. Round cell infiltrates about some ducts and nests (Fig 5).

This case represents the typical pathological changes of chronic cystic mastitis or which Cheate classifies as cystiphorous desquamative epithelial hyperplasia.

**CASE** Hospital N 71473 Mrs E H aged 37 years, with child aged 6. A lump had been noticed in the right breast for 8 months, swelling in the right shoulder and arm for year and "pusulent" discharge from the nipple for 5 weeks. She had been treated with chemotherapy, hot applications, alcohol dressings, and balsam of Peru. Examination revealed freely movable mass the size of lemon, fixed at the nipple. Cord like strands could be felt radiating outward from the tumor mass. At operation mastectomy was done. There was noted considerable find of scars to "peristaltic" character encircling into the mass from the glandular structure. Numerous cut sections of the breast revealed multiple blue, dome like cysts. Microscopically there is some sclerosis of the fibrous tissue stroma of the breast and several cysts, varying considerably in size, lined with cuboidal epithelium which in some areas are several layers thick. No evidence of malignancy was noted (Fig 6).

**CASE 3** Hospital No 822 J Mrs C H aged 3 years, married, 10 years, and has 3 children. Patient complained of marked intermittent tenderness in the left breast beginning about 6 months previously. Four months before admission she noticed large lump in the dependent portion which disappeared in week by the use of sling support, and the application of heat. Three weeks before admission she noticed bloody discharge from the nipple and since then there has been an occasional drop from it from day to day. Examination revealed slight sanguineous discharge



Fig. 7. Abscess in surface. Terminal ducts with epithelial hyperplasia. Other sections showed dilated papilloma and inflammation in surface vessels.



Fig. 8. Abscess dilated duct with papilloma and carcinoma. Lower center groups of epithelial cells (carcinoma).

in the left nipple no palpable mass, no tenderness. Roentgen examination revealed areas of a cystic non-descriptive epithelial hyperplasia which in the absence of a mass and bleeding from the nipple permitted a presumptive diagnosis of papilloma to be made. Operation consisted of simple amputation of the breast. Multiple sections through the specimen showed an increase in the fibrous tissue of the breast with a slight brown and red discolored area underlying the nipple measuring 1 centimeter in diameter a phloxed dilated blood vessel. Microscopic sections of breast showed small clear mass. There is dilatation of the ducts with blood in some and cellular debris in others. Occasionally one sees fibrous projections into lumen of duct covered with epithelium about which there is fibrosis and round cell infiltration (Fig. 3).

CASE 2. Hospital No. 70414. Mrs. M. V. aged 54 years has 4 children aged 35 and 36 years. She gives a history of some pain and slight purulent discharge from the right nipple of 10 weeks duration. Examination revealed a tender mass in the right breast with a purulent drainage from the nipple which was slightly ulcerated. A roentgen examination revealed the findings to be those of a cystic condition with degeneration that was probably malignant. At operation a radical amputation of the breast was done because of a pre-operative diagnosis of Paget's disease. Grossly the specimen presented a hard irregular mass measuring on section 2.5 by 2 by 5 centimeters. There was considerable cystic degeneration none of the cysts measuring more than 1.5 centimeters in diameter. The tumor was not encapsulated and from its periphery radiated pinkish white strands of rather dense tissue into the surrounding stroma suggestive of malignancy. Microscopic sections show dilatation of ducts with epithelial hyperplasia and the formation of small papillomas projecting into the lumen. There is no invasion of the stroma. In other areas there is epithelial hyperplasia with a filling of the lumen of the duct and with definite periductal round cell infiltration. This case is definitely precancerous as evidenced by the rapidly growing epithelial cells (Fig. 4).

CASE 3. Hospital No. 87002. Mrs. J. P. aged 34 years single. Patient had had a swelling in her left breast 7 months previously which disappeared following a serous discharge from the nipple. This occurred on two occasions. Four or five weeks before admission the discharge became sanguineous. There was some soreness and a pain which radiated down the medial surface of the left arm to the wrist. Examination revealed a brownish pigmentation of the skin of the breast no asymmetry. A small mass was palpable in the upper inner quadrant and when pressure was made upon this mass a brownish fluid escaped from the nipple. No adenopathy, no retraction of the nipple, no tenderness were noted. Operation consisted of an excision of the tumor with a zone of the breast tissue. The specimen revealed several ducts distended with a brownish thick fluid matter suggesting changed blood. In one of these dilated ducts a glistening grayish soft papillary tumor hung from the wall measuring about 0.5 centimeter in diameter. Sections show a papilloma of duct but no evidence of malignancy (Fig. 5).

CASE 6. Hospital No. 80030. Mrs. M. H. aged 50 years has 2 children, three miscarriages. She had a bloody ooze from the right nipple of 1 1/2 months duration. A few drops of blood in 4 hours occurred at first later to change in consistency to a serous thin fluid. For 1 or 2 years she had noticed some itching of the nipple but no pain until 2 days before admission. Examination revealed no lumps in the breast. At operation several pieces of tissue were excised showing it to be very fibrous and of a firm consistency. No gross evidence of inflammation or tumor formation could be found in the specimens although one small thin area of connective tissue was thought to be a cyst wall. Microscopically in one of the numerous sections is seen a distended duct with a projection of granular tissue some of the epithelial cells of which appear to invade but they do not impress as being of active growth. The growth was believed to be benign (Fig. 6).



Fig. 9. Terminal duct showing marked epithelial hyperplasia. Other areas showed dense malignancy. Classically the case as one of Paget's disease.

**CASE 7.** Hospital No. 950. Mrs. M. M. age 68 years, had no children, menopause occurred 7 years ago, patient stated that at that time she had some bleeding from the right nipple then she noticed nothing until 6 months ago when there appeared a lump in the breast. This increased in size but softened after some bleeding from the nipple. A hard, small, slightly tender mass was felt to the left and below the right nipple. Operation consisted of excision of some of breast tissue with the nipple. On sectioning the specimen, there was found underlying the nipple a rounded solid, grayish granular mass located 2 cm. or so in close proximity to the ducts. The ducts showed several areas of cystic dilatation and contained dark red blood or soft grayish caseous matter. Microscopic sections show of cystic dilatation with epithelial hyperplasia of ducts with low grade papillary formation. In one area at least there was thought to be an extension beyond normal confines. The pathologist considered this to be ductal carcinoma of low grade malignancy (Fig. 7). A frozen section in the operating room as diagnosed papilloma with no evidence of malignancy. A report from the laboratory of the complete routine examination of the tumor disclosed the extension of the tumor beyond its normal confines. A radical operation for the removal of the breast was not done but the patient shows no evidence of recurrence at the present time.

This case exemplifies the great danger one occasionally encounters in the surgery of breast tumors.

**CASE 8.** Hospital No. 70849. E. F. aged 50 years, single, nurse. In June, 1927 she experienced an insect bite on the nipple of her right breast which was followed by redness, swelling, and tenderness, which disappeared in a few days. A few months later there occurred discharges of some brown fluid from this nipple. Her physician advised cleaning of the nipple with alcohol. Four months before



Fig. 8. Papilloma of duct, the epithelium of papilloma large and hyperchromatic. This breast in other sections presented malignancy.

admission there was discharge of considerable amount of blood. 7 weeks before admission the breast was accidentally struck with resulting swelling, tenderness, and considerable hemorrhage from the nipple. Examination showed a large flattened lump which was not very tender and which seemed to be attached to the pectoral fascia. The nipple was not inverted and its pit was filled with serosanguinous fluid. The skin over the upper pole of the tumor seemed to be attached to it. The right axilla presented no palpable glands. A radical amputation of the right breast was done at operation. The specimen showed some the size of her ring just below the nipple, such as hard, fixed, and on cross section presented a very dense appearance of malignancy. On microscopic examination the breast appears to have been the seat of mastitis. There are old sclerotic areas present with cyst like cavities and papillary projections. In addition there is very definite malignancy outside of the area just described. The malignant cells are seen to produce small cords but nests and glands are also produced. There is very definite extension of the breast fat (Fig. 8). This case presents the interesting feature of having papilloma present as well as carcinoma in another area of the breast.

**CASE 9.** Hospital No. 40273. G. S. aged 55 years had child, menopause 7 years ago. A lump in the right breast was first noticed 3 years ago. This was removed by physician. One year later another lump appeared and during the past 3 months it has increased rapidly in size. There is peripheal bleeding from the nipple and it is at times the circumference there as found an excoriated eruption

about the right nipple. A hard mass was present in the lower left quadrant of the right breast which was fixed to the muscles and skin. In the outer and upper quadrant there was another mass which was softer and was not fixed. A gland was palpable in the axilla. Operation consisted of a radical breast amputation. Pathologically the skin surface of the specimens showed two distinctive lesions. One was about an area which was considered to be the areola and nipple. The nipple was flattened out and appeared to be a continuation of the surrounding skin. It was differentiated, however, by a thin, shiny gray epithelium, somewhat suggestive of scar tissue. This area was surrounded by a series of pin point sized bleeding points. The other lesion of the surface was a large contracted scar measuring 5 by 3 centimeters. The scar was adherent to a large, solid, hard granular mass which, on sectioning, proved to be a large, solid, hard, granular mass with definitely infiltrating bodies. On one edge of the mass was a cystic cavity 1.5 centimeters in diameter, filled with blood. On the tumor side of the cyst were papillary projections into the cyst cavity. The latter were apparently continuations of the tumor tissue. Sections through the nipple area revealed a marked prominence of the ductal structures. Three enlarged lymph nodes were found, one of which was solid, grayish, firm, and with glistening cut surfaces, suggesting malignancy. Microscopically the sections showed skin inflammation under the epiderm but no typical Paget's cells. There was a suggestion of malignant cell invasion of the epiderm but this was not certain. The ducts of the nipple showed epithelial hyperplasia and extension beyond confines. Section of the tumor showed carcinoma of the ducts (Fig 9). This case typically exemplifies the pathological picture of Paget's disease and its close association with a carcinoma of the ducts lying immediately beneath the nipple. The treatment of Paget's disease of the nipple should always be radical and the case treated as a malignancy from the beginning.

CASE 10 Hospital No S2179 Mrs L P aged 71 years menopause at the age of 51, 8 children. Three years ago she noticed an inversion of her right nipple and about 6 months later a lump appeared in the right breast. Three weeks before admission to hospital she bruised her right breast which was followed by slight tenderness and a serous discharge from her right nipple. Examination revealed the nipple to be inverted and from it there was a serous discharge. A mass was present in the medial upper quadrant which was freely movable and not fixed to the skin. Some tenderness was noted on pressure. A simple breast amputation was performed. No frozen section was made and the axilla was not disturbed. The specimen had a retracted nipple in its center. A hard, rounded somewhat nodular and not definitely circumscribed mass could be palpated within 1 centimeter from the nipple which had a slight attachment to the skin. Cross section revealed a mass 3.5 centimeters in diameter. Its cut surface showed a firm pink and gray granular friable tumor tissue with small hemorrhages and many areas of apparent necrosis at its center. The larger ducts contained much light yellowish green exudate. The microscopic pathology of many sections showed no evidence of malignancy. The stroma of the breast in these sections was translucent did not appear to be as dense as hyalin. Other sections show undoubted malignancy. The condition is believed to be a cystoma which has undergone malignancy, the epithelial cells of the new growth appearing at times to be spindle shaped (Figs 10 and 11).

The etiology of the bleeding from the nipple in this case is problematical but trauma was pre-



Fig 11 Carcinoma in breast which presented the intra ductal papilloma seen in Figure 10. Note duct filled with malignant epithelium in lower right corner.

sumably responsible. The clinical features of the case were sufficient to warrant the surgeon making a pre-operative diagnosis of a possible malignancy. At operation, however, the tumor was not sectioned or a frozen section was not requested. The final diagnosis from the laboratory was received after the patient had left the hospital. Again, the importance of an immediate frozen section in the operating room cannot be stressed too strongly.

#### SUMMARY

A careful study of the pathology of these ten cases reveals the interesting changes and gradations that occur in the breast from the very early cystiphorous desquamative epithelial hyperplasia state through to the neoplastic state of carcinoma as has been described by Cheate and Cutler.

Cases 1 and 2 present the very early cystiphorous state and Case 4 with beginning neoplasia gives the history of there having been a so called purulent discharge from the nipple. The history of such a discharge is not described by Cheate as being one of the early symptoms of this pathological state or of the early neoplasia state but he describes such a discharge as being associated with carcinoma. A discharge of blood may occur

in any of the stages as shown by this analysis even in Case 1 which is a very early cystophorous lesion.

The 4 cases of malignancy in this group had a palpable tumor in the breast and serous or bloody discharge from the nipple. In Case 7 the discharge occurred 12 years previously and was followed by a carcinoma. These 4 cases exhibited pathological evidence of a malignant condition involving the ducts of the breast and one of these cases was associated with Paget's disease of the nipple.

Clinical examination revealed no tumors in the breasts of Cases 3 and 6 but in the 8 remaining cases, masses varying in size, consistency and sensitivity were noted.

The pathological examination of the specimens revealed papilloma to be single or multiple and when multiple they were found to be in separate ducts. Contrary to the opinion of some surgical pathologists, it was determined quite definitely that a papilloma may become malignant. Case 7 presented the history and physical findings of a simple ductal papilloma, was surgically treated as such, confirmed by microscopic frozen section but later there was found to be a carcinoma in the routine laboratory examination. Pathological examinations in Cases 9 and 10 show the neoplastic carcinomas with epithelial changes in the papillomas.

The analysis of these cases also confirms the often neglected surgical axiom that a lump in the breast should be removed as soon as it is noticed, regardless of the discharge from the nipple. Clinical signs of a carcinoma are necessary before a diagnosis of malignancy can be made and before these signs develop the diagnosis of a palpable tumor can be made only microscopically. It is important therefore for patients having a tumor in the breast with a discharge from the nipple to be operated upon in a hospital with a competent pathologist at hand to make an immediate microscopical frozen section of the tumor. If found to be malignant the surgeon should be prepared to perform immediately a complete radical amputation of the breast.

Inasmuch as papillomas are at times multiple and a carcinoma may be obscured in another area of the breast, it is our opinion that the entire gland should be regarded with suspicion for immediate as well as for future pathological conditions. For this reason the surgical procedure of choice for all cases of bleeding or discharge from the nipple is a mastectomy. If a microscopical frozen section of a demonstrable tumor shows malignancy the radical operation can then be done.

# CONCLUSIONS

The study of these cases although small in number leads us to the following conclusions:

1. The pathological classification of benign and malignant tumors of the breast seems greatly facilitated by following the work of Cheate and Cutler.

2. A discharge of blood from the nipple with no palpable tumor in the absence of a history of trauma, is presumably caused by a papilloma of a duct or ducts of the breast.

3. A so called purulent discharge from the nipple is found to be associated with a cystophorous desquamative epithelial hyperplasia as well as with carcinoma.

4. A discharge of serum or blood from the nipple with or without a palpable tumor is a surgical condition.

5. Mastectomy should be the surgical procedure of choice as papillomas may be multiple, may be present in more than one duct, and contrary to some theories, papillomas may become malignant.

6. An immediate microscopical frozen section of the tumor should be made in the operating room and if this discloses a malignancy an immediate radical operation should be performed.

7. Routine laboratory study of multiple microscopical sections of the breast is essential in discovering their pathological lesions.

8. A carcinoma of the breast may be hidden and obscured in one area of the breast while the clinical symptoms of a papilloma predominate in another part of the breast.

9. Paget's disease of the nipple can be considered as always being associated with carcinoma and demands a radical amputation of the breast.

# REFERENCES

1. ALLEN, F. E. Seriginous discharge from the nipple and its significance in relation to cancer of the breast. *Ann. Surg.* 1910, 9, 97.
2. BRONCKHOFF, JOSEPH C. The clinical and pathological differential diagnosis of diseases of the female breast. *Am. J. M. Sc.* 1908, 35, 57.
3. IDEM. The clinical picture of dilated ducts beneath the nipple frequently to be palpated as doughy areas like tumor—the anastotic tumor of the breast. *Surg. Gynec. & Obst.* 9, 1, 36, 436.
4. IDEM. Chronic cystic mastitis of the mamma, non-encapsulated cystic adenocarcinoma type. *Ann. Surg.* 1909, 90, 886.
5. IDEM. The blue-domed cyst in chronic cystic mastitis. *J. Am. M. Ass.* 1909, 91, 996.
6. IDEM. Cancer of the breast. *Surg. Gynec. & Obst.* 1909, 40, 739.
7. IDEM. The changing clinical picture of lesions of the breast. *Am. J. M. Sc.* 1910, 70, 37.
8. IDEM. Border line breast tumors. *Ann. Surg.* 1911, 91, 35.
9. IDEM. Personal communication, 1914.

10. Idem Lesions of the female breast. *Binnie's Regional Surgery*, Vol. 1, Sec. 27, 571
11. CHESTER, G. J., and CUTLER, MAX. Tumors of the Breast. Philadelphia: J. B. Lippincott Co. 1937
12. DEWEE, J. B., and McFARLAND, J. The Breast. Philadelphia: P. Blakiston's Son & Co. 1917
13. GREENOUGH, ROBERT B. and SIMMONS, LUCIANNE C. Papillary cyst adenoma of the breast. *Ann Surg.*, 1907, 45, 188
14. GROSS, I. W. Quoted by Greenough and Simmons
15. HERTLER, ARTHUR I. Surgical Pathology of the Mammary Gland. Philadelphia: J. B. Lippincott Co. 1911
16. LEWIS, DEAN. Bleeding nipples. *Surg., Gynec. & Obst.*, 1916, 22, 666
17. MILLIF, I. M., and LEWIS, DEAN. The significance of a sero hemorrhagic or hemorrhagic discharge from the nipple. *J. Am. M. Ass.*, 1923, 81, 1651, 1657
18. ROSSMAN, WILLIAM L. Carcinoma of breast. *Murphy's Clinics*, 1915, 4, 247
19. SAAR, J. REINHOLD VON. Leber Cystadenoma Mammæ und Miltstistis Chronica Cystica. *Arch. f. klin. Chir.*, 1907, 84, 2, 3
20. TOLLEF, PIERRE. The bleeding nipple. *Med. J. & Rec.*, 1905, 11, 517

## OBSTETRICAL ANALGESIA WITH PENTOBARBITAL SODIUM

### THE LEUCOCYTE RESPONSE DURING THE PERIPIUM

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RECENT clinical observations and laboratory studies point to a number of commonly used drugs which occasionally produce neutropenia in susceptible individuals. The nature of the mechanism by which they depress the activity of the bone marrow is not clear, although the evidence seems to indicate that compounds containing the benzene ring are the chief offenders. Thus, amidopyrine and arsphenamine are among the more common drugs, the exhibition of which has been followed by neutropenia.

The administration of several popular proprietary mixtures of drugs which contain both barbiturates and coal tar products, such as allonal (allylisopropylbarbituric acid plus amidopyrine) and amyltal compound (amyltal plus amidopyrine) has been reported to have been followed by neutropenia. In the minds of many physicians this has brought under suspicion the derivatives of barbituric acid as a group.

With the exception of those which contain the benzene ring, (i.e. phenobarbital) there is no evidence that the derivatives of barbituric acid themselves cause neutropenia. Barbiturates have been used extensively and in relatively large doses over a period of nearly 4 years at the Boston Lying-in Hospital. There have been no deaths from neutropenia during this period, neither have there been any cases in which the diagnosis of neutropenia due to drug poisoning could be made. In this connection it is of interest to review in more detail a consecutive series of patients who have received such medication during labor.<sup>2</sup>

Our series consists of 3,502 delivered patients, 1,242 of whom received pentobarbital sodium (sodium ethyl (1-methyl butyl) barbiturate) alone, and 2,350 of whom were given pentobarbital sodium in combination with scopolamine. The drugs were given in sufficient quantity to produce analgesia and amnesia during labor. When scopolamine was used it was given by hypodermic injection. The pentobarbital sodium was given by mouth (rarely by rectum) in total dosage varying from 3 to 25½ grains. Few patients received less than 6 grains. The larger doses were divided, rarely more than 6 grains being given at once. The period over which the drug was given varied as the labor, in many, a single dose sufficed, in others, divided doses were given over a period of 48 or more hours.

There were no cases of typical agranulocytosis or neutropenia among the 3,502 patients. In the whole series there were 11 deaths, most of which were primarily obstetrical. We do not believe that neutropenia caused by pentobarbital was a factor in any of them. In order that this may be clear, every death in the group is briefly abstracted.

CASE 1. No 1069. A multipara of 31 delivered normally after a short labor during which she received 9 grains of pentobarbital. The postpartum course was entirely afebrile and uneventful until she died suddenly on the eleventh day of massive pulmonary embolism.

CASE 2. No 11175. A primipara of 25 at term suffered from severe rheumatic heart disease with both mitral and aortic lesions. She was admitted in labor on the edge of congestive failure. Three grains of pentobarbital were given

<sup>2</sup>Since this work was begun a series of patients who had been given pentobarbital sodium during labor were reported by Hardwick and Randall (*J. Am. M. Ass.* 1934, 102, 159-160). The total number of patients reported was 59, only 5 of whom received more than 9 grains.

<sup>1</sup>From the Department of Obstetrics, Medical School, Harvard University, and the Boston Lying-in Hospital.

of the drug. Their findings—Studies of the blood from this group of patients give no evidence of the production of a leukopenic condition with the amounts of pentobarbital-sodium administered—is entirely substantiated by our results.

and she was delivered by low forceps when the cervix was fully dilated. There was more than the usual blood loss at delivery and the patient, as put back to bed in mild failure. She improved until the third day when suddenly she developed multiple pulmonary emboli from which she died, 24 hours later.

CASE 3. N. 772. A primipara of 36, as delivered normally. During the course of labor she had received 9 grains of pentobarbital. On the fifth postpartum day she developed signs of severe postpartum sepsis from which she died on the eleventh day. White blood cell counts on the fifth, sixth, and tenth days were respectively 7,000, 9,800, and 4,000.

CASE 4. N. 074. A 40 year old primipara was delivered by cesarean section after long test of labor during which she received 4½ grains of pentobarbital. White blood cell counts on the third and fifth days were 24,600 and 4,000, respectively. She died unexpectedly on the eighth day of pulmonary embolism.

CASE 5. No 6731. A quadripara of 30 with placenta previa as delivered by cesarean section. There was profuse postpartum hemorrhage from which she died in spite of transfusion and hysterectomy. She had received 9 grains of pentobarbital.

CASE 6. No 7770. Labor as induced during the thirty eighth week in multipara because of increasingly severe toxemia. The patient was delivered normally after 3 hour labor during which she was given 6 grains of pentobarbital. There was a delayed postpartum hemorrhage from which she died, 9 hours after delivery in spite of packing of the uterus and two transfusions.

CASE 7. No 0663. A primipara of 36 was delivered by low forceps after short labor during which she had received 6 grains of pentobarbital. She died on the twentieth postpartum day of bilateral cerebral tuberculous pneumonia. Ten white blood cell counts in the first 8 days varied between 1,000 and 20,000.

CASE 8. No 84. A primipara of 34 was delivered by low forceps after labor during which she received 9 grains of pentobarbital. Eight hours after delivery she suddenly became cyanotic, with rapid pulse and respirations. She died on the second postpartum day of pulmonary embolism.

CASE 9. N. 0084. A tripara of 24 was delivered by cesarean section after test of labor during which she received 5 grains of pentobarbital. She died on the twentieth postpartum day of sepsis. White blood cell counts on the sixth, eleventh, and sixteenth days were, respectively, 1,000, 25,000, and 9,000.

CASE 10. No 8. Because of severe neglected toxemia which had failed to respond to treatment, labor was induced in an obese primipara of 27 at term. After an 8 hour labor during which she had received 9 grains of pentobarbital, she was delivered when the head had been on the perineum for hours without progress. The baby was very large (weighed 3 ounces) and the delivery of the shoulders very difficult. The patient died 4 hours postpartum of shock and hemorrhage in spite of transfusion.

CASE 11. N. 6044. A primipara at term was delivered by transverse cervical cesarean section after long test of labor, the latter part of which was febrile. During labor she had been given 8 grains of pentobarbital. The patient developed peritonitis and bronchopneumonia. On the sixth day she would breathe down and she emaciated her milkteeth. She died on the seventh postpartum day, 24 hours after secondary closure of the wound. White blood cell counts were as follows: days following induction, 24,400, third day, 1,600, 500 sixth day, 4,700 and 3,800, and on the day of death, 5, 30. Differential also did

polymorphonuclears in excess of 64 per cent, except for the count of 3,700 when they were 50 per cent.

The last case is the only one in the whole series in which the white blood cell count was low. We do not believe, for several reasons, that the administration of pentobarbital had anything to do with the low white count in this case. In the first place, the severity of the infection in itself would adequately explain the low count. Besides, there was a marked initial leucocytosis 48 hours after administration of the drug, which is not characteristic of the neutropenia which follows the administration of drugs. Finally the count was never extremely low and the percentage of neutrophils was never below 50.

Since in the course of routine postpartum care, white blood cell counts were done only upon patients with complications in the puerperium in whom there were clinical indications, it is impossible to state that there were no instances in which the white cell count was abnormally low. However one can state that there were no patients with clinical symptoms referable to neutropenia.

With the possibility in mind of low white counts following use of pentobarbital in patients without symptoms, a series of white blood cell counts were made during the puerperium upon a group of patients who had received the larger doses of the drug during labor. The counts are done when possible on the second and fifth days following delivery and once or twice thereafter. This interval following administration of the drug would seem to be the most likely one in which to find neutropenia if the medication had caused it. In known cases of idiosyncrasy to antipyretics, such as amidopyrene, the symptoms have usually followed the use of the drug within 1 or 2 days. Neutropenia usually reaches its maximum within 5 to 6 days. In addition, the bulk of experimental evidence would tend to place the life of the mature circulating granulocyte at 3 to 5 days. Thus, if inhibition of pentobarbital had inhibited the bone marrow from releasing granulocytes into the circulation, the diminution in their number in the circulating blood would already be marked by the second postpartum day and extreme by the fifth day. The subsequent counts were made to rule out a rather unlikely delayed effect. The results are presented in Table I.

With the exception of the one case of fatal peritonitis and bronchopneumonia already presented in detail, and in which the low white count was undoubtedly the result of an overwhelming infection, there were no abnormally low white counts. It is perhaps of interest that the average

TABLE I—WHITE BLOOD CELL COUNTS IN PUERPERIUM FOLLOWING THE ADMINISTRATION OF PENTOBARBITAL DURING LABOR

Dose of pentobarbital	Number of cases	First 3 days			4th to 6th days			7th to 14th days		
		Maximum	Minimum	Average	Maximum	Minimum	Average	Maximum	Minimum	Average
7½-10 grains	16	25210	9210	13000	24050	8450	11500	16450	6000	9250
10-12 grains	23	21850	11300	16450	20900	8600	11800	18350	6150	10900
12-15 grains	8	20000	10500	15500	21700	3600	13500	18000	1800	10100

Differentials were made in all cases. The percentages of neutrophils were high or normal in all cases except for this one in which the polymorphonuclears were never less than 10 per cent. This case is reported in detail elsewhere in the paper.

white count increased as the dose of pentobarbital increased. This may be explained in that the patients who received the larger doses had longer, and on the whole, more difficult labors, following which one would expect more reaction.

#### SUMMARY

A series of 3,592 cases is presented in which relatively large doses of pentobarbital were given during labor. None of them developed clinical

symptoms of neutropenia. Reported white blood cell counts during the puerperium in a series of patients who had received the larger doses of pentobarbital revealed that the drug was not followed by lowered white count, and indeed, that it did not interfere with the normal leucocytosis of the puerperium. Finally, there would appear to be no ground for fear that pentobarbital is followed by neutropenia when given in adequate therapeutic dosage during labor.



## EDITORIALS

### SURGERY GYNECOLOGY AND OBSTETRICS

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OCTOBER, 1933

#### CHOLECYSTECTOMY WITHOUT DRAINAGE

**W**IDESPREAD interest in cholecystectomy without drainage has introduced new problems in the field of biliary surgery. Omission of the drain after simple cholecystectomy permits a smooth and rapid convalescence, less foreign body reaction with its consequent adhesions, decreased likelihood of dehiscence of the abdominal wound and absence of an irritant drain rubbing on ligatured bile ducts and blood vessels, inviting late leakage.

Unfortunately the universal desire to try new methods results in a backward swing of the pendulum. In the hope that the good results of cholecystectomy without drainage may not be lost in the reverberations against the procedure, a recapitulation of the indications and technique may be timely. The success of the method is granted but a few failures have evoked a storm of criticism the latter have been due, in so far as I am able to interpret them to injudicious and inexperienced efforts in this new field.

It would seem that the indications for omitting the drain in cholecystectomy should

be evident. Recent or old perforations of the gall bladder with resultant abscess formation, acute cholecystitis, and adherent omentum or viscera which must be freed from the gall bladder before the latter can be removed, warrant drainage in almost every instance. Infected edematous tissue invites drainage, lest our judgment of the degree of subsiding inflammation be underestimated. Spillage of gall-bladder content however minor and all instances of surgical exploration of a bile duct, demand provision for drainage. There should be no doubt of drainage in all the instances cited but if doubt persists, the safe dictum is, "when in doubt, drain."

Technically cholecystectomy without drainage is on a par with thyroidectomy without drainage. When Wallace I. Terry promulgated thyroidectomy without drainage, he changed the technical details of the operation. The same principles advocated by Dr. Terry must be adhered to if we are to omit the drain when performing cholecystectomy. In only certain cases may operation be done without drainage and certain features of the technical detail must be assiduously observed. The major requisite is a dry operative field. All severed blood vessels and bile ducts must be securely ligated; the smaller sizes of ligature material should be used; mass ligation of tissue is contra indicated and approximation of tissue without tension is pre-requisite. Raw surfaces may not be left exposed in the liver bed and meticulous attention to small hematomata is necessary.

When subserous cholecystectomy is performed after the injection of salt solution under the serosa of the gall-bladder wall, the

edema thus produced permits easy enucleation of the gall bladder, but it also may result in late oozing of blood or bile from the small vessels compressed by the edema. When the edema is absorbed, the vessels open and drain. Fortunately, the vessels are small and do not drain long, but they may ooze sufficiently to militate against the success of non-drainage. If no drain is used, these vessels must be ligated even though they do not bleed during the operative period. The same holds true for the small bile ducts which empty into the side of the gall bladder from the liver bed. As these anomalous structures are present in nearly 6 per cent of all persons, they offer a danger of considerable magnitude. Of course other anomalous biliary ducts must be searched for, but though they occur in at least 10 per cent of bodies they are not so frequently overlooked, for they are of larger caliber. Anomalous blood vessels are even more numerous, yet are rarely even searched for. If any bile ducts are encountered that seem to be anomalous, they should be exposed from their origin in the liver to their termination in the gall bladder, bile duct or duodenum. The cystic duct should be exposed from the gall bladder to the common hepatic duct by bluntly dissecting the peritoneum and fat from it, for unless it is amply exposed, anomalies of the ductal and vascular tree may be traumatized without recognition, to become a source of late leakage. Gentle handling of tissue and atraumatic technique are vital to the success of cholecystectomy without drainage. The hurried operation, strenuously performed, is no procedure to be followed by omission of the drain.

The anesthetic is important, for when the patient must be heavily drugged in preparation for the anesthesia, and in cases in which ether is used as the anesthetic agent, bile flow from the liver is decreased. Then the smaller biliary

ducts do not drain when severed and therefore they are not secured by ligature. Local infiltration, spinal and gas anesthetics do not interfere with this function of the liver.

In spite of the limitations thus placed upon cholecystectomy without drainage, it has been possible to close the abdomen without drainage in 82 per cent of 241 simple cholecystectomies for gall stones. In only one instance has omission of the drain been regretted, yet in 2 cases drains have failed to function. In both of the latter, the drain itself became walled-off, and probably induced the bile lake which surrounded the terminal tip of the drain.

Cholecystectomy without drainage is a new field in biliary surgery and promises to be a satisfactory procedure, but it cannot be done successfully unless our technique is altered and of course, unless our selection of cases is judicious.

STANLEY H. MENTZER

### DIAGNOSTIC STUDY OF OBSCURE ABDOMINAL COMPLAINTS

**D**ESPITE all attempts at accuracy, diagnosis in obscure abdominal complaints is still inexact and far removed from the goal that medical men are seeking. While the art of administering treatment, both medical and surgical, can gradually be acquired by the individual, the making of diagnoses in obscure abdominal conditions usually requires co-operative effort, and while the treatment of disease makes a strong appeal to the more material side of the physician, the making of diagnoses seems to appeal more to the spiritual and intellectual side. Consequently, the making of diagnoses usually presents more difficulties than does therapy.

Vague abdominal complaints which persist present a large field for diagnostic study and are frequently slighted by the physician until

the clinical picture becomes sufficiently clarified to clinch the diagnosis. Often this is late in the progress of the disease. In other cases exploratory operations, which are more or less useless, are performed to clarify the situation.

With all the recent advances in roentgenography many of these cases, if adequately studied can be elucidated. Unfortunately even with all these modern aids, in many cases diagnosis still remains obscure. The technique of studying these patients is still expensive, but the method of approach to these obscure conditions seems definitely crystallised since we can portray so much on the X ray film. We have adopted a definite routine in these patients and this routine visualises the whole abdomen—the urinary tract, the biliary tract and the gastro-intestinal tract, and as well the subarachnoid space, if there is any suggestion of its involvement.

First a flat picture of the abdomen is made and then an excretory urogram. A series of pictures of the gall bladder is followed by a

series of the gastro-intestinal tract and of the colon after a barium enema. In this way the three important tubular systems within the abdomen are studied with almost scientific accuracy and as most complaints arise from disturbances in these parts, the patient's condition or complaints may thus be clarified with some certainty.

In cases in which the roentgenographic studies indicate that the complaints are not connected with these tubular organs and in which there is adequate suspicion that the abdominal pains are referred, a lipiodol subarachnoid injection is indicated for diagnosis and localisation of a possible spinal cord neoplasm. This procedure may clarify a previously perplexing clinical picture. All in all, adequate and complete use of the available diagnostic methods in abdominal complaints is not made at the present time. It is definitely our duty to study all obscure cases completely in the manner here again outlined.

EDWARD BAKER.





NATHANIEL ALLISON  
1876-1932

# MASTER SURGEONS OF AMERICA

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## NATHANIEL ALLISON

NO one member of the medical profession in this country has had more influence on the development of modern orthopedic institutions than Nathaniel Allison. As professor of orthopedic surgery in three of our leading medical schools at various intervals during the last 15 years, and as chief of the orthopedic services which these schools controlled, his influence was widespread and of the utmost importance in their development. Those who were fortunate enough to work under him experienced a stimulus rarely felt. Always alert to the newer developments in surgery of the bones and joints, and interested in investigative work, he made all who came in contact with him feel the urge to improve the whole field of orthopedic surgery. His own investigations were most valuable, but only with the realization of the volume of work produced by his associates, often at his suggestion and always with his fullest co-operation, can the scope of his influence be appreciated.

Dr. Allison's influence was not confined alone to investigative work in surgery of the bones and joints, he excelled also in organization. In the problems of hospital organization, of work by committees, whether of a medico-political trend or of the most scientific import, his ability was outstanding. Scientific meetings large or small, were led by his quiet but firm influence. He was able to bring together a conglomeration of divergent viewpoints, and thus develop order out of chaos.

Dr. Allison was born in St. Louis. His father was the son of Dr. Nathaniel Allison of Mexico, Missouri, and his grandfather's influence led him to enter the practice of medicine. His early education was obtained in St. Louis. This was followed by a period of study in the United States Military Academy in West Point. He entered Harvard in 1894 and graduated in medicine there in 1901. After an internship at the Boston Children's Hospital and a period of service with Dr. Edward Bradford in Boston he returned to St. Louis in 1904, where he built up his reputation as an orthopedic surgeon of international repute. He was married to Marion Aldrich of Chicago in 1909.

Dr. Allison's earlier work in St. Louis led to the development of the orthopedic service at the Barnes Hospital and the teaching of that branch in the Medical School of Washington University. In 1915 he was with the American Ambu-

lance Corps at Neuilly France, and later with the American Expeditionary Forces he served in Base Hospital 21 at Rouen. In the autumn of 1917 when special consultant services were organized, he was second in charge of the work of organizing the care of fractures, and the work in the advanced areas was under his supervision. This was a task requiring constant vigilance, tact, and wisdom and the efficiency with which it was carried out testifies to his skill and understanding. Returning from France he served for a time in Walter Reed Hospital as assistant director of the surgical service. He was awarded the Distinguished Service Medal and was finally discharged from the service as colonel which rank he held in the Medical Reserve Corps until his death.

After Dr Allison's discharge from the army he was sent to Rome as representative of the Medical Department at the Inter Allied Congress of Surgery. Having accomplished this mission he returned to St. Louis and resumed his practice, and a professorship at Washington University officiating as Dean of the Medical School. In 1923 he returned to Boston as chief of the orthopedic department of the Massachusetts General Hospital and on the death of Dr Robert W. Lovett he was made professor of orthopedic surgery in the Harvard Medical School. He also served as chief of the staff of the New England Peabody Home for Crippled Children, and in many other ways made his influence felt in the medical community of Boston.

In 1929, with the reorganization of the Medical Department of the University of Chicago and the Billings Memorial and Allied Hospitals, a chief of the Orthopedic Service was sought and Allison was asked to serve in this capacity and again the result was one of the best organized and equipped orthopedic services in the country. While there, in 1930 he was stricken, and although he recovered and resumed his post for a period of many months in 1931 he never completely resumed his former activity.

His influence was wide and many organizations not mentioned owed to him a great deal for his share in their development. His pleasing personality and his ability to meet people of widely divergent viewpoints and bring them together when necessary must be regarded as one of his outstanding characteristics. Those who worked with him always felt that he was governed only by a desire to see progress in orthopedic diagnosis and practice. Never without a plan to improve conditions when necessary he was greatly in demand when all sorts of difficult tasks had to be performed. Although to many his work may not have seemed difficult yet there must have been numerous times when the multiplicity of these tasks were harder on him than was realized thus helping to bring to an untimely end one of the most useful careers in modern orthopedic surgery.

RALPH E. CHORLEY

# EARLY AMERICAN MEDICAL SCHOOLS

## BAYLOR UNIVERSITY COLLEGE OF MEDICINE

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**B**AYLOR University, the oldest university organized in Texas, was chartered in 1845 by the Republic of Texas during the Presidency of Anson Jones and for 90 years has occupied front rank in the educational affairs of the Southwest. The academic department has for many years been located in the centrally situated city of Waco, Texas, the various professional schools are in Dallas.

When, 35 years ago, a small group of physicians in North Texas determined that opportunity for medical education should be offered ambitious young men of this section, prevented by transportation difficulties and economic stress from attendance at apparently distant institutions, the establishment of a medical school in the then thinly settled and geographically isolated region was as surely a pioneer undertaking as had been similar ventures in eastern and middle western states a half century before.

After a long series of conferences, organization was effected in September, 1900, at a public meeting of interested civic and professional individuals.

The first term of the new school, which was chartered by the State of Texas as the medical department of a projected but non-existent institution, the University of Dallas, opened on November 10, 1900, in a building which had formerly housed a Jewish synagogue.

To the astonishment of the new faculty, about 60 students registered for the courses, but whatever optimism may have been engendered by this apparent justification of the venture was soon dampened by a series of minor catastrophes.

A present perusal of the old minutes of the business meetings of the faculty during the organization's first year suggests to the reader the scenario of a melodrama with frequent interpolations from the book of Job. The equipment was meager, the teaching staff was small, and, although enthusiastic and earnest, its members with a few exceptions were unaccustomed to pedagogy. The majority of the local medical profession scoffed at the enterprise and freely predicted its failure. No state law permitting the legal use of cadavers for dissection and demonstration existed, and while the local authorities were sufficiently complaisant to render grave robbing unnecessary, the securing and transportation of anatomical material immediately became a problem. A well authenticated incident relates the midnight experience of one R. W. McFerran, a member of the first class, who volunteered to transport a body, unclaimed by friends or relatives, from the city morgue to the dissecting room with the tacit consent of those in charge. Mr. McFerran had only a horse and buggy for the purpose, and there



The medical school building, left, and City Hospital, where ward rounds and clinics were first conducted, in 1903





Baylor University of Medicine and Baylor University Hospital, 935

were dressed the corpse carefully and placed it in proper sitting position beside him in the vehicle. Half way to the school building on turning a corner the body lurched and its hat blew off. A kindly policeman called out to the student 'Your friend' lost his hat' and as the officer ran behind the equipage with the head gear in his hand, the frightened embryo scientist plied the whip with vigor shouted 'be sure you can have it' and, history records, reached medical sanctuary safely.

In December 1900, three members of the faculty staged a revolution, took charge of the building by an overnight coup d'état, changed the name and organization of the school, and engaged a policeman to guard the premises in support of the new government. The remainder of the faculty were successful in securing an injunction against the junta forbidding interference with the proceedings of the medical department of the University of Dallas and a deputy sheriff dissolved the revolution. Fifteen diplomas were granted at the close of the first term, the recipients of which had obtained advanced standing from courses which were taken in other institutions.

In 1901 the minutes record, a permanent teaching staff of 17 was selected. In the allocation of professorships surgery was assigned to Drs. Joe Becton, Sr. and B. E. Hadra; anatomy to Dr. J. M. Inge; physiology to Dr. A. C. Bell; pediatrics, to Dr. A. F. Beckdole; obstetrics, to Dr. J. H. Florence; gynecology and rectal diseases, to Dr. V. P. Armstrong; and gynecology to Dr. J. E. Gilcreest. Dr. Elbert Dunlap, who is now head of the department of gynecology, as made professor of materia medica and genito-urinary diseases. Dr. Edward H. Cary, who later became dean, and who still holds the chair of ophthalmology and otolaryngology was made professor of diseases of the eye, ear, nose and throat. Dr. Charles M. Rosser, one of the original founders group, he is now professor of clinical surgery was made dean of the faculty.

Drs. Gilcreest, Becton, and Inge were well known and well trained Texas surgeons of the period who, living in neighboring communities, gave the infant institution helpful privilege and at considerable inconvenience lectured regularly to its classes. It is a matter of some personal interest to this recorder in view of the fact that Baylor is now one of the twelve schools of the country including a complete section on proctology that this earliest faculty based instruction in the subject.

In 1901 the school building was destroyed by fire and classes were conducted in the basement of the city hall until the conclusion of the term, when 9 graduates were awarded diplomas.

In 1903 the institution, in common with others throughout the United States, came to the crossroads of its destiny. For no other reason than that the plan was common and well understood the school had been organized as a stock company. The American Medical Association, in pronouncements issued in 1903, very correctly discouraged this type of organization and also insisted that university affiliation and teaching hospital connection are essential to those medical schools which were destined to survive.

Overtures were made to Baylor University looking toward affiliation and on June 30, 1903, an agreement was entered into whereby the stock company was dissolved and its properties conveyed to the university which assumed a protectorate over the school. In 1900, it became an integral and coordinate part of Baylor University. Dissolution of the stock company and university affiliation satisfied two of the three criteria set up; the third requirement was met when, in 1900, the institution now known as Baylor University Hospital, which has been built on the grounds of the Good Samaritan Hospital, Dr. C. M. Rosser's private institution, opened its doors and, operated jointly with the school, afforded an excellent teaching hospital connection.

The Rockefeller Foundation survey in 1908-1910 which disclosed widespread defects in the medical education of that time and resulted in a marked reduction in the number of existing medical schools, stimulated Baylor to necessary local corrections and additions, and in 1916 the Council on Medical Education of the American Medical Association awarded the institution the complete recognition which has been continuously maintained.

The faculty now number 144, 34 ranking as professors. The school hospital plant now repre-

sents a capital outlay of nearly two and one-half millions of dollars. Administration is under the direction of Dr. J. F. Kimball, vice-president of Baylor University in charge of professional schools, Dr. Walter H. Moursund, professor of bacteriology, has been dean of the faculty since 1923. The student body averages 360, the freshman class being limited to 100, degrees have been awarded 1,065 students, who now practice their profession creditably not only throughout the Southwest but in all parts of the United States.



# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

THE present volume of the *Surgical Pathology of the Peritoneum* by Hertzer deals with the surgical pathology of the peritoneum and has 304 pages with 201 excellent illustrations by Tom Jones and Barlow. A comprehensive index is included and a short bibliography is given at the end of each chapter.

Professor Hertzer writes in a very clear and forceful style. It is apparent from this monograph that the author not only has interpreted a liberal amount of experimental work but has drawn freely on his large clinical experience. In reading the work, one is pleasingly impressed with the many practical applications and deductions.

From the viewpoint of a general surgeon, it was very thoughtful of the writer to restrict the discussion of the histopathology to a brief review of the important and characteristic changes. This conservative manner of presentation seems to reside almost entirely with writers of wide clinical experience. One has the impression that the author overemphasized the benignity of adhesions when he stated that undesirable clinical effects of permanent adhesions are negligible (p. 55). This seems somewhat incongruous in the face of the teaching that from 50 to 65 per cent of cases of acute intestinal obstruction are due to postoperative bands and adhesions.

The chapters on peritonitis are written exceedingly well and should be read by every young surgeon. Tumors of the peritoneum, mesentery, omentum, and retroperitoneal space are considered in one chapter. Still other chapters are devoted to diseases of the omentum, mesenteric thrombosis and specific peritonitis.

This monograph is a distinctly worth while effort.

R. W. McVicar

THE seventh edition<sup>1</sup> of Macleod stands at a text of physiology is remarkable for the comprehensive revision which has been undertaken. The contributions of those assisting in the present edition have been skillfully elided into a harmonious whole, with little of the overlapping and repetition which is so frequently present in works produced by a group of collaborators. Many of the new concepts which

have been developed in the 5 years which have elapsed since the previous edition are included without a material increase in the number of pages of this already large volume.

One of the chief merits of this text, prizing equally its use in the hands of students or for general reference is the clarity of its presentation and the ease and pleasure with which it may be read. Most subjects are set forth in a detailed manner, in a style not ambiguous or likely to be found confusing. The 377 illustrations are for the most part clear and useful. A rearrangement of the contents, by which the treatment of the nervous system is placed last, introduces the student to those aspects of physiology which are perhaps most easily assimilated and allows of an orientation in the subject before introducing muscle and nerve which is often found more difficult. An excellent feature which would bear adoption in other texts is the rather comprehensive list of references which includes not only other texts and monographs but original papers in the various fields. From the American point of view there is perhaps a disproportionate attention to English and continental literature while many significant American contributions are neglected.

While complete in many aspects, this edition, like those of previous years, entirely neglects certain phases of the subject. The term "Biochemistry" is now dropped from the title and the arm of this work is to present physiology with biochemistry retained only so far as it is necessary to the elucidation of problems of animal function. The general subject matter covered, however, is much the same as in previous editions. Reproduction is still omitted the liver is not given a section but is treated under various headings in the chapters on metabolism. A number of less important omissions detract from the completeness of the volume. The index is less complete than is desirable for one who uses the text primarily for reference.

To the medical student perhaps the most serious lack is the failure to summarize the evidence concerning various phases of the subject and to draw specific conclusions. The volume is so large and the material in each section so voluminous, that while one can scarcely comment adversely on the absence of didactic presentation, brief recapitulations might bind the various chapters more closely and aid the student in obtaining a perspective of the science of physiology as a whole.

A. C. I.

<sup>1</sup> *GENERAL PHYSIOLOGY OF THE PERITOINEUM*. By Arthur E. Hertzer, M.D. 7th ed. Philadelphia: Saunders & Co., London: J. B. Lippincott & Co.

<sup>2</sup> *PHYSIOLOGY OF MAN*. Macleod, J. R. Macleod, W. B. Macleod. 7th ed. F&P. 1935. 12 vol. 56 Lanes. N.Y. The C. V. Mosby Co. 1935.

THE popularity of Sutton's well known work<sup>1</sup> is attested by the fact that this is the ninth edition. The author has adopted his son as a permanent literary associate and the work is now published under the joint authorship of Drs Sutton and Sutton.

The book has always been an easy one to read as it is printed in large, legible type, on an excellent quality of paper. In this edition, 27 new conditions have been described and many others, including coccidioidal granuloma, tularemia, and the treatment of syphilis completely revised.

The illustrations are even more plentiful than they have been in the past, and in this edition there are 1310 illustrations and 11 colored plates. Many new photographs have been inserted to replace old ones and there are many photomicrographs.

The bibliography printed at the end of each subject has been added to and brought completely up to date. It has always been a feature of the work and is even more comprehensive than it has been in the past.

The only criticism that can be offered is that the book is growing so large that with further editions it may be necessary to publish it again in two volumes.

The authors are to be congratulated on the painstaking way the book has been compiled and I heartily recommend it to all practitioners who are interested in the subject of dermatology.

EDWARD A. OLIVER.

IN the seventh edition of *Physical Diagnosis*<sup>2</sup> by Elmer and Rose, the section on electrocardiography, silicosis, and diagnostic methods has been added to and revised. The first 543 pages are devoted to the physical examination of the entire normal body. Each of the standard diagnostic procedures is covered completely before the next one is considered. For example, the much neglected art of inspection is well described, the beginner completes his technique of inspection of the body as a whole, the head, neck, chest, abdomen, and extremities before proceeding with palpation, percussion, and auscultation, which sections are covered in a similar manner. This plan is especially suitable for the student who is a beginner in the study of physical diagnosis.

The second part of the book (340 pages) is devoted to diseases of the respiratory and circulatory organs. The section on electrocardiography and abnormalities of the heart beat is well written and contains numerous tracings. The chapter on "Radiology" in physical diagnosis is an essential part of any modern text on this subject. The text is abundantly illustrated and is recommended to both student and practitioner.

CLARENCE J. McMULLEN.

<sup>1</sup> DISEASES OF THE SKIN. By Richard L. Sutton M.D., Sc.D. LL.D. F.R.S. (Edin.) and Richard L. Sutton Jr. A.M. M.D. L.R.C.P. (Edin.) 6th ed. St. Louis Mo. The C.V. Mosby Co. 1935.

<sup>2</sup> PHYSICAL DIAGNOSIS. By Warren P. Elmer B.S. M.D. and W. D. Rose 7th ed. St. Louis Mo. The C.V. Mosby Co. 1935.

THE manual<sup>3</sup> by Conybeare ranks with the best of the rather numerous manuals of diabetes that are available, its outstanding qualities are brevity and clearness. The author has outlined in 94 pages the general considerations which govern the physician's treatment of diabetes and, in an appendix of 22 pages, which may be obtained separately, he has provided for patients, detailed instructions with reference to practical points upon which successful self-care depends.

Detailed or technical discussions of the more theoretical and biochemical aspects of diabetic metabolism and a bibliography are intentionally omitted. The dangers of over-nutrition and excessive insulin dosage are stressed. By allowing 100 to 140 grams of carbohydrate the author believes that the diet can be made reasonably palatable and that special diabetic foods are not required. With such carbohydrate allowance he believes that there is no conclusive evidence that the amount of fat needed to furnish a maintenance diet predisposes to arteriosclerosis. The value of examinations of the urine four times daily (in the early morning, before luncheon, before dinner, and at bedtime) is emphasized.

To the physician who desires concise information as to modern conservative management of diabetes and to the intelligent patient this book will be helpful.

WALTER H. NADLER.

IN a ponderous volume<sup>4</sup> of 1028 pages of which 36 are index, Gradwohl apparently has attempted to produce an encyclopedia of clinical laboratory methods. Matters of technique are in fine print, interpretation and discussion of results are in larger type. "The standard technic of accepted procedures is given in strictest detail, together with an interpretation of all data obtained by standard tests," says the author in his preface. There is no attempt at selection and no definite recommendation of any one method. For example, 10 qualitative tests for albumin and 7 for sugar in the urine are described. The descriptions of technical procedures are models of brevity and are, usually, adequate and clear. In each case a constant formula is followed. The reagent and its preparation, the technique of the test, the changes that constitute a positive result with attention to possible misleading reactions. In those tests in which a quantitative result is the goal, the formula and a concrete example of its application are given.

A chapter on blood chemistry of 80 pages contains a useful table of the composition of normal human blood with the diseases or pathological states in which changes in each constituent may be encountered. The author is especially interested in hematology and the chapter on this subject, which occupies 180 pages, is useful and stimulating. Special

<sup>3</sup> MANUAL OF DIABETES. By J.J. Conybeare M.C. M.D. (Oxon.) F.R.C.P. London. Oxford University Press. 1935.

<sup>4</sup> CLINICAL LABORATORY METHODS AND DIAGNOSIS. A TEXTBOOK OF LABORATORY PROCEDURES WITH THEIR INTERPRETATION. By R. B. H. Gradwohl M.D. St. Louis Mo. The C.V. Mosby Co. 1935.

attention is given to the technique and significance of the Schilling tests. This volume contains sections on the diagnosis of rabies, tests for pregnancy and hypersensitiveness, chemical analysis of milk, identification of pathogenic fungi, the making of autogenous vaccines etc. The following chapter headings give an idea of the comprehensiveness of this book: Parasitology and Exotic Pathology, 95 pages; Bacteriological Applications to Clinical Diagnosis, 155 pages; Serology, 49 pages; Basal Metabolism, 7 pages; Postmortem Examinations, 4 pages; Tissue Cutting and Staining, 35 pages; Preparation of Museum Specimens, 16 pages; and Toxicologic Technique, 36 pages.

There are 324 illustrations in black and white and 24 colored plates. Numerous tables and charts are useful adjuncts to the text. The declared purpose of the author in writing this volume was "to help the clinician, the laboratory worker, and the medical student to learn laboratory diagnosis." The book is larger and more comprehensive than is necessary for medical students, but it should be a very useful addition to the working library of any active laboratory.

J. P. SWANSON

THE general plan of the fifth edition of Chouder's book, *Method of Treatment*, has not been changed from that of his first edition. The book is still planned to furnish an outline of all methods of treatment in internal medicine. The revisions made represent the author's own ideas entirely in reference to given drug, diet, or form of treatment, etc.

The book is divided into 4 parts. Part I is devoted to general therapeutics, the methods used in treatment. In this section rest, drugs, diet, and hydrotherapy are discussed. The author describes in detail the method of preparation and the procedure to follow in carrying out the various forms of treatment.

Part II discusses special therapeutics, the application of therapeutics to particular diseases. The author gives full description of the application and the results to be expected from the various treatments he has outlined.

There are numerous illustrations throughout the book, showing instruments, describing technique, and a method of procedure for the treatments outlined.

This book, because it is a combination of materia medica and therapeutics, should be a valuable reference in any physician's library.

CLIFFORD J. BARNHART

THE excellent textbook on urology by Essendrieth and Kohnke has been revised to include the more recent advances in diagnostic and therapeutic urology. An important addition is the chapter on renal calculi, covering in most complete manner

METHODS OF TREATMENT. By LEON CHOUDEUR, M.D. 5th ed. St. Louis, Mo. The C. V. Mosby Co. 1931.

TEXT BOOK ON UROLOGY AND ITS CONNECTIONS WITH NEPHROLOGY. By DANIEL H. ESSENDRIETH, M.D. and HARRY C. KOHNKE, M.D. 3d ed. 1930. Philadelphia: J. B. Lippincott & Co. 1931.

the differential diagnosis of cholelithiasis. Transurethral electro-resection of various types of bladder neck obstructions has been considered in the light of the pathological anatomy and pathological physiology of prostatic hypertrophy. The chapters on anatomy of the kidneys and ureters, injuries of the kidney and cystic disease of the kidneys are especially commendable. Another similar text that I have seen is so ably and adequately illustrated. While the work is somewhat too gross for the average medical student during his academic career, it is one that could well be used for reference during his school days and later found most useful during his years of clinical application.

VICTOR J. O'CONNOR

IN the second edition of Copeman's book, which first appeared in 1933, many revisions and additions, particularly in the section on therapy have been made. The use of gold salt therapy, histamine, bromocriptin, intra-vascular calcium, and short wave diathermy is discussed. The book is a general survey of the various rheumatic diseases. Chapters are devoted to the discussion of acute rheumatic fever, chorea, acute muscular hepatitis, and fibrositis, sciatica and neuritis, rheumatoid arthritis, osteoarthritis, and spondylitis. The treatment of these various afflictions is discussed in some detail in Part III which makes up 1/3 of the book. A chapter is devoted to prognosis. The author draws from his own rich experience, particularly in evaluating the various therapeutic measures. The book is very readable and should be of great value to the man in general practice.

J. RALPH MILLER

IN a 302 page monograph Guggisberg covers the subject of vitamins with special reference to obstetrics and gynecology as well as the field in general. The work is an enlargement and revision of his contribution as it originally appeared in Hildebrandt, *Biologie und Pathologie des Weibes* in 1929. The subject material is evenly divided. There is a general chapter on vitamins and more specifically the relation of vitamins to pregnancy, labor, the puerperium, the newborn, their relation to the sex organs, and internal secretions. Various sub-chapters of general biologic interest are included, such as relation to growth, constitution, nutrition, malignant tumors, tuberculosis, and wound healing. There is much repetition in the reading matter and much that is given is not new.

The author distills the alphabetical nomenclature of vitamins and suggests that they be named according to physical, chemical, and physiological properties. He follows out the classification of Wastenburg and Funk, based largely on fat and water solubility. The vitamins of special interest in obstetrics and gynecology are the B complex consisting of B<sub>1</sub> and

THE TREATMENT OF RHEUMATISM IN GENERAL PRACTICE. By H. J. COPEMAN, M.A., M.D. 2d ed. London: H. K. Lewis. 1935. 10s. 6d. By H. J. Copeman, M.A., M.D. 2d ed. London: H. K. Lewis. 1935. 10s. 6d.

THE RHEUMATISM AND ITS TREATMENT. By DANIEL H. ESSENDRIETH, M.D. and HARRY C. KOHNKE, M.D. 3d ed. 1930. Philadelphia: J. B. Lippincott & Co. 1931.

B, C, D, and E. There are many references to experimental work, but the author cautions the reader in drawing conclusions from such work and applying them directly to the human species. It appears that, if there is a congenital factor as regards vitamins, the deficiency exists merely from birth for such factors were not supplied during pregnancy. Further disturbances in growth are aggravated only when the deficiency is continued. Reactions, however, are reversible. It is interesting to note in this connection that there is no fetal rickets, but if there is a lack of vitamin D supplied by the mother, a rachitic tendency in the newborn child could very quickly develop. The author is familiar with all of the world's literature, in fact has contributed much to the subject from his own laboratory. An excellent bibliography, including the world's literature from 1929 to date, is appended.

W B SERBIN

THE book by Colwell entitled *The Method of Action of Radium and X-rays on Living Tissues*<sup>1</sup> meets a need and it may be said at the outset that it succeeds in bridging the gap which it intends to hedge. It is surprising how well the author covers a tremendous field of experimental work in this comparatively small volume. His own experience in this field, based on the contributions made by himself and in co-operation with Svdnev Russ, enables him to review the material very critically.

All branches of biology, biological chemistry, histology, serology, and clinical treatment, which are connected with the action of radiation on living tissues, are considered. In the first chapter the author gives a review of the effect of radiation on the cell. He considers the changes produced by radiation on different cell organs (cell membrane, cytoplasm, cytoplasmic inclusions, and nuclei). In this chapter he reviews the observations and interprets them from the point of view of the most modern knowledge of colloidal chemistry of the cell.

The second chapter covers the observations made on the chemical action of radiation. Here he considers the effect of rays on colloids, on oxidation and reduction phenomena as far as they are related to biological reactions. He also reports in this chapter the effect of radiation on enzymes. A large part is devoted to the effect of radiation on autolysis. The effect of rays on lipoids of the cell and on cholesterol is also reported. Special consideration is given to glutathione because of its fundamental importance in cell oxidation. This is followed by the report of Crabtree's work on the effect of radium radiation on tissue oxidation and carbohydrate metabolism. A short discussion of the results of radiation on the chemical composition of proteins is included.

In further chapters the action of radiation on the

reticulo-endothelial system and some immunity reactions are reported. The effect of radiation on antibody formation and its dependence on the quality and dosage of the radiation are reported. These considerations constitute a basis for the important chapters which deal with the *effect of radiation on tumor growth* since the immunity reactions are at least partly due, on the one hand, to the reticulo-endothelial system and, on the other hand, some careful investigations support the assumption that tumor growth is regulated by the function of the reticulo-endothelial system.

In the fifth chapter, "Radiation and Resistance to Tumor Growth," these questions are discussed extensively. The effect of radiation on tumor growth is considered from the point of view of the effect of radiation on the isolated cells, this means on tissue cultures *in vitro* before grafting these cells. Furthermore, the effect on tumor cells in animals and the effect on the reticulo-endothelial system of the bearer of the tumor are reported. It is particularly important from the clinical point of view that there are also experimental observations which indicate that the different amounts of radiation in the cells produce different results, so that a certain amount produces immunity reactions against further tumor growth (which may be due to certain contents of the tumor cells), whereas too large amounts of radiation seem to destroy these substances. The question of the importance of the reticulo-endothelial system for the growth of tumor metastases or for the resistance against this growth is critically discussed.

While this chapter deals mostly with grafted tumors, the last chapter, "The Action of Radiation on Malignant Tumors," gives the results of radiation effect on malignant tumors in man. It is based primarily on the classical work of Lacassagne and Monod, which is extensively reported, and the possibility of explaining the results on the basis of present knowledge is discussed. In logical connection with this material, the question of radiosensitivity of tumor tissues is considered.

In reporting this extensive material and considering the many special questions, the author never loses the broad general biological view. He attempts to show what clinical application can be made of this material. In this manner the book gives an excellent review of the present status of all questions which are related to radiotherapy, giving a safe, non-speculative basis for the application of experimental knowledge to clinical treatment.

This work serves as a basis for new experimental work, but it is more than a convenient guide for the experimental worker. It gives to the clinical radiologist the means of understanding and interpreting some of his observations and gives him new stimulation. For this reason, the book should be read by every radiologist who wishes to administer his treatment on a sound and intelligent basis.

MAX CUTLER.

<sup>1</sup> THE METHOD OF ACTION OF RADIIUM AND X-RAYS ON LIVING TISSUES. Hector A. Colwell M.B. Ph.D. M.R.C.P. D.P.H. London Oxford University Press 1935.

## BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgments must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and at spare moments.

**THE SUBCUTANEOUS MIND.** By Cyril Burt, M.A. D.Sc. (Oxon.) London: Oxford University Press, 1935.

**EXTENSION CIRCUITOSA.** By Enrique Rueda Rueda. Glos. Pablo Rueda Societade Editora Medica Libraria, 934.

**THE DISEASES OF THE ENDOCRINE GLANDS.** By Herman Zondek, M.D. (Berlin). 3d ed. rev. and col., trans. lated by Carl Pincus, M.D. (Brynar). M.R.C.S. (Eng.), L.R.C.P. (Lond.) Baltimore: Williams Wood & Co. 925.

**THE INTERNATIONAL MEDICAL ANNUAL, A YEAR BOOK OF THERAPY AND PRACTITIONER'S INQUIRY.** 935, Fifty-third year. Baltimore: Williams Wood & Co. 1935.

**CHEMICAL TUBERCULOSIS.** Edited by Benjamin Goldwag, M.D. F.A.C.P. P.A.P.H.A. Vol. and Philadelphia: F. A. Davis Co. 1935.

**NATIONAL MEDICAL MONOGRAPHS. ONSCHWARTZ FOR THE GENERAL PRACTITIONER.** By J. P. Grosshull, B.S. M.D. F.A.C.S. Edited by Marion Finkels, M.D. New York: National Medical Book Co. Inc. 935.

**GYNECOLOGICAL AND OBSTETRICAL TUBERCULOSIS.** By Edwin M. Jamison, B.S. M.D. Philadelphia: Lea & Febiger 1935.

**A SURVEY OF ROSTONAL ANATOMY.** By T. B. Johnston, M.B. Ch.B. 3d ed. Philadelphia: Lea & Febiger, 1935.

**THE PRINCIPLES AND PRACTICE OF SURGICAL MONITOR.** By Charles D. Lockwood, A.M. M.D. F.A.C.S. and John A. Walter, M.D. F.A.C.S. In collaboration with Mildred E. Newton, B.S. R.N. 3d rev. ed. New York: The Macmillan Co. 935.

**THE THEORY AND PRACTICE OF ANESTHESIA.** By M. D. Kowatshy, M.A. M.D. B.Ch. (Cantab.) with foreword by J. W. Magill. London: Hutchinson Scientific, 1935.

**THE AMERICAN ILLUSTRATED MEDICAL DICTIONARY. A COMPLETE DICTIONARY OF THE TERMS USED IN MEDICINE, SURGERY, DENTISTRY, PHARMACY, CHEMISTRY, NURSING, VETERINARY SCIENCE, BIOLOGY, MEDICAL PROGRAMS ETC. WITH THE PRONUNCIATION DERIVATION AND DEFINITION.** By W. A. Newman Dowland, A.M. M.D. F.A.C.S. 17th ed. rev. and col. With the collaboration of E. C. L. Miller, M.D. Philadelphia and London: W. B. Saunders Co. 1935.

**NEW AND NONOFFICIAL RECIPES, 1935. CONTAINING DESCRIPTIONS OF THE ARTICLES WHICH STAND ACCEPTED BY THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION ON JANUARY 1, 1935.** Chicago: American Medical Ass. 1935.

**ANNUAL REPORT OF THE REPORTS OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR 1934 WITH THE COMMENTS THEY HAVE APPEARED IN THE JOURNAL.** Chicago: American Medical Ass. 934.

**HUGH OWEN THOMAS, HIS PRINCIPLES AND PRACTICE.** By D. McCrac Arden, M.A. M.B. Ch.B. (Ed.) F.R.C.S. (Ed. and Eng.) London: Oxford University Press, 1935.

**THE ALPHABETIC PLAN OF THE AMERICAN JOURNAL OF CULTURAL BACKGROUND.** By Wallace Thomas Corlett, M.D. L.R.C.P. (Lond.) Springfield, Ill. and Baltimore, Md. Charles C. Thomas, 935.

**DISEASES OF THE THYROID GLAND.** By Arthur Z. Hertler, M.D. With chapters on Hospital Management of Goiter Patients by Victor E. Chesky, M.D. 3d rev. ed. St. Louis, Mo.: The C. V. Mosby Co. 1935.

**THE MEDICAL ANNUAL GENERAL INDEX AND REVIEW FOR THE TEN YEARS 1925 TO 1934.** Baltimore: Williams Wood & Co. 935.

**HORMONES AND STIMULANTS AND THEIR HYPOTHYROIDISM-LATTERS: DIFFERENTIALS FOR BIOLOGICAL AND CLINICAL USES.** By Dr. Bernhard Zondek. 3d ed. ed. Wm. Johns Hopkins, 1935.

**THE LIVERPOOL MEDICAL-CHIRURGICAL JOURNAL.** H. G. OWEN THOMAS. CENTENARY NUMBER. Vol. 43, part 2, 935. Liverpool: Medical Institution. London: H. K. Lewis & Co. Ltd.

**THE CIRCULATORY SYSTEM AND THE CIRCULATORY CIRCULATION.** AN ANATOMICAL, EXPERIMENTAL, AND CLINICAL INVESTIGATION. By Edw. Ash. Upchurch. Supplement 6 to ACTA PHTHIOLOGICA ET NEUROLOGICA. Copenhagen: Levin & Munksgaard, 1935.

**NUTRITION OF MOTHERS AND CHILD.** By C. Ulrich Moore, M.D. M.Sc. (Med.) F.A.C.P. 4th rev. ed. Philadelphia and London: J. B. Lippincott Co. 935.

**DISEASES OF THE LIVER, GALL BLADDER, DUCTS AND PANCREAS, THEIR DIAGNOSIS AND TREATMENT.** By Samuel Weiss, M.D. F.A.C.P. New York: Paul B. Hoeber, Inc. 1935.

**A TEXT BOOK OF FRACTURES AND DISLOCATIONS, COVERING THEIR PATHOLOGIC DIAGNOSIS. TREATMENT.** By Kellogg Speed, S.B. M.D. F.A.C.S. 3d ed. thoroughly rev. Philadelphia: Lea & Febiger, 1935.

**AGENTS OF DISEASE AND HOST RESISTANCE, INCLUDING THE PRINCIPLES OF IMMUNOLOGY, BACTERIOLOGY, MYCOLOGY, PHOTOMIOLOGY, PARASITOLOGY AND VIRUS DISEASES.** By Frederick P. Coy. Springfield, Ill. and Baltimore, Md. Charles C. Thomas, 935.

**TRANSACTIONS OF THE SOUTHERN SURGICAL ASSOCIATION. Vol. 47. FORTY-SEVENTH ANNUAL MEETING.** Edited by Allen Oschner, M.D. New York: Paul B. Hoeber, Inc. 1935.

**HISTOLOGICAL DATA.** By Dr. Oscar Ivanovsky. Buenos Aires: Imprenta Americana, 934.

**LA BIOGEOGRAFIA, EN EL ESTADO DE LAS ANTICIPACIONES DEL VORAZ.** By Raul Puga Blanco and Federico Giron Caputo. Montevideo: Imp. "El Siglo Veintiuno," 1935.

**THE PNEUMONOTOLOGICAL (SILVANO) LITERATURE. LA LAYO OF 934. INTERNATIONAL ABSTRACTS, EXTRACTS AND REVIEWS OF THE PNEUMONOTOLOGICAL AND THEIR ASSOCIATED DISEASES AND SUBJECTS.** By George O. Davis, M.D. Ella M. Balaban, and Joseph L. Early. Chicago: Chicago Medical Press (Not Inc.), 1935.

**PREVENTIVE MEDICINE AND HYGIENE.** By Milton J. Sosenow. 6th ed. New York and London: D. Appleton-Century Co. 1935.

**HUMAN PATHOLOGY. A TEXTBOOK.** By Howard T. Kanner, M.D. With an introduction by Samuel Hexter, M.D. 4th rev. ed. Philadelphia and London: J. B. Lippincott Co. 935.

**APRILIA, CLINICAL AND PSYCHOLOGICAL STUDY.** By Theodore Wernberg, M.D. and Katherine E. McBride, Ph.D. New York: The Commonwealth Fund. London: H. K. Lewis & Co. Ltd.—Oxford University Press, 1935.

# CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

ROBERT B. GREENOUGH, Boston, *President*

DONALD C. BALFOUR, Rochester, *President-Elect*

HOWARD C. NAFFZIGER, *Chairman*, THOMAS F. MULLEN, *Secretary*, *Committee on Arrangements*

## PROGRAM FOR THE 1935 CLINICAL CONGRESS IN SAN FRANCISCO AND OAKLAND

### CLINICAL CONGRESS PROGRAM IN BRIEF

#### *Monday, October 28*

- 9 00. Clinics in San Francisco hospitals.
- 9 30. Hospital conference—Fairmont Hotel, Ballroom
- 2 00. Clinics in San Francisco hospitals
- 2 00. Hospital conference—Fairmont Hotel, Ballroom
- 2 00. Surgical films—Fairmont Hotel, Red Room
- 5 00. State and Provincial Executive Committees—Fairmont Hotel, Gray Room
- 8 15. Presidential meeting—War Memorial Opera House

#### *Tuesday, October 29*

- 9 00. Clinics in San Francisco hospitals.
- 9 30. Section on ophthalmology and otolaryngology, scientific session—Fairmont Hotel, Gray Room
- 9 30. Hospital conference—Fairmont Hotel, Ballroom
- 10 00. Surgical films—Fairmont Hotel, Red Room
- 2 00. Clinics in San Francisco hospitals
- 2 00. Hospital conference—St. Mary's Hospital.
- 2 00. Surgical films—Fairmont Hotel, Red Room
- 2 00. Fracture conference—Fairmont Hotel, Ballroom.
- 8 00. Hospital conference—St. Mary's Hospital.
- 8 15. Scientific session, general surgery—Auditorium, Veterans' Building

#### *Wednesday, October 30—Oakland Day*

- 9 00. Clinics in Alameda County hospitals.
- 9 30. Hospital conference—Fairmont Hotel, Red Room
- 9 30. Surgical films—Fairmont Hotel, Ballroom.
- 2 00. Clinics in Alameda County hospitals.
- 2 00. Surgical films—Fairmont Hotel, Ballroom
- 2 00. Hospital conferences—University of California Hospital and San Francisco Hospital
- 8 00. Community health meeting—Exposition Auditorium
- 8 15. Scientific session general surgery—Auditorium, Veterans Building

#### *Thursday, October 31*

- 9 00. Clinics in San Francisco hospitals.
- 9 30. Section on ophthalmology and otolaryngology, scientific session—Fairmont Hotel, Gray Room
- 9 30. Hospital conference—Providence Hospital, Oakland
- 10 00. Surgical films—Fairmont Hotel, Red Room
- 1 30. Annual meeting—Fairmont Hotel, Ballroom
- 2 00. Clinics in San Francisco hospitals
- 2 00. Hospital conference—Samuel Merritt Hospital, Oakland.

- 3 00. Cancer symposium—Fairmont Hotel, Ballroom
- 8 15. Scientific session, general surgery—Auditorium, Veterans' Building

#### *Friday, November 1*

- 9 00. Clinics in San Francisco hospitals
- 9 30. Section on ophthalmology and otolaryngology, scientific session—Fairmont Hotel, Gray Room
- 10 00. Surgical films—Fairmont Hotel, Red Room
- 10 00. Hospital conference and tour of Alameda County hospitals.
- 11 00. Meeting of new Fellows, class of 1935—Fairmont Hotel, Ballroom.
- 2 00. Clinics in San Francisco hospitals.
- 2 00. Surgical films—Fairmont Hotel, Red Room
- 2 00. Conference on industrial medicine and traumatic surgery—Fairmont Hotel, Ballroom
- 8 15. Convocation—Scottish Rite Auditorium

THE surgeons of San Francisco and Oakland have prepared a program of clinics and demonstrations that will provide a complete showing of the clinical activities in all departments of surgery in that great medical center on the Pacific coast during the twenty-fifth annual Clinical Congress of the American College of Surgeons, October 28–November 1. The Committee on Arrangements has been assured of the hearty co-operation of the clinicians at the two medical schools and twenty-seven hospitals that will participate in the program.

The clinical program, published in the following pages, will be further revised and amplified during the weeks preceding the Congress. Operative clinics and demonstrations in the hospitals are scheduled for the morning and afternoon of Monday, October 28, beginning at 9 o'clock and for the mornings and afternoons of each of the four following days. The real program of the Congress will be published daily—a complete and accurately detailed program that will be posted in the form of bulletins at headquarters each afternoon for the succeeding day. The same material will be issued in printed form the following morning.



Special features of the clinical program include: (1) Cancer clinics demonstrating the treatment of cancer by surgery, radium and X-ray; (2) fracture clinics demonstrating modern methods of treatment; (3) clinics in traumatic surgery demonstrating the newer methods of rehabilitation of injured patients by surgery and physiotherapy.

During the Congress the hospital ship *Relief* of the U. S. Navy will be docked at a convenient point on the waterfront. Clinics on board ship will be given on Tuesday morning by Commander Horace R. Boone and associates, and arrangements will be made for an inspection of the ship by the visiting surgeons and their friends during the Congress.

#### SPECIAL PROGRAMS AT HEADQUARTERS

A conference on fractures, under the auspices of the College Committee on the Treatment of Fractures, will be held in the Gold Ballroom of the Fairmont Hotel on Tuesday afternoon at 2 o'clock. A detailed program is presented in the following pages.

Under the auspices of the College Committee on the Treatment of Malignant Diseases a symposium on cancer will be presented in the Gold Ballroom of the Fairmont Hotel on Thursday afternoon following the annual meeting of Fellows. The symposium will concentrate on the standard accepted methods for the treatment of cancer. A report on five year results of therapy compiled by the Department of Clinical Research containing the gathering of statistics on this subject from clinicians in various parts of the United States and Canada during the past several years, will be included. A detailed program is presented in the following pages.

The annual conference of the Board on Industrial Medicine and Traumatic Surgery will be held in the Gold Ballroom of the Fairmont Hotel on Friday afternoon at 2 o'clock. The program, which appears in the following pages, includes a report of the activities of the College in conducting investigations and surveys among industrial establishments during the past year in continuation of the work done along these lines during the past five years.

#### EVENING MEETINGS

Programs for the five evening sessions as prepared by the Central Executive Committee are presented in the following pages. At the presidential meeting on Monday evening in the War Memorial Opera House following the address by the retiring president, Dr. Robert B. Greenough of Boston, the new officers elected at the 1934

Clinical Congress will be inaugurated—Dr. Donald C. Balfour Rochester, Minn., president; Dr. Arthur W. Allen, Boston, and Dr. John A. Guze, Winnipeg, vice-presidents. Dr. George Cline of Cleveland, Chairman of the Board of Regents, will deliver the annual oration on surgery, his subject being "The American College of Surgeons—Past, Present and Future." This address will include a tribute to the life and work of the late Dr. Franklin H. Martin.

Scientific sessions will be held in the Auditorium of the Veterans Building on Tuesday, Wednesday and Thursday evenings, at which eminent surgeons of the United States and Canada will present and discuss papers on surgical subjects of timely importance.

The annual convocation of the College will be held on Friday evening in the Scottish Rite Auditorium, at which the 1935 class of candidates will be received into Fellowship. The president, Dr. Donald C. Balfour of Rochester, Minn., will deliver his inaugural address on this occasion, and Dr. Robert Gordon Sproul, B.S., LL.D., president of the University of California, will deliver the Fellowship address.

#### OPHTHALMOLOGY AND OTOLARYNGOLOGY

The committee in charge of the section on surgery of the eye, ear, nose and throat has arranged a program of ophthalmological and otolaryngological clinics and demonstrations at the hospitals and medical schools, as published in the following pages. Also scientific sessions are to be held at the Fairmont Hotel on Tuesday, Thursday and Friday mornings, at which clinical papers are to be presented by visiting surgeons and discussed by local clinicians. The programs for these scientific sessions appear in the following pages.

#### MEETING OF NEW FELLOWS

Candidates for fellowship in the American College of Surgeons, class of 1935, will assemble in the Gold Ballroom of the Fairmont Hotel at 1:30 p.m. on Friday for the necessary instructions previous to receiving their fellowships and to sign the fellowship roll.

#### COMMUNITY HEALTH MEETING

Following its established custom and in recognition of an obligation to the public to provide authoritative information on modern surgery, better hospitals and the prevention of disease a community health meeting will be held on Wednesday evening at 8 o'clock, under the auspices of the American College of Surgeons, in the Exposition Auditorium. A program appropri-

ate for the occasion consisting of brief interesting talks on scientific medicine, health, and hospitals, including a motion picture film on a medical subject of interest to the laity, will be presented, as follows

DONALD C BALFOUR, M D , Rochester, Minnesota, presiding  
 Invocation  
 Address of Welcome HOWARD C NAFFZIGER, M D , San Francisco, Chairman, Committee on Arrangements  
 Message of Greeting JACOB C GEIGER, M D , San Francisco, Director of Public Health  
 The American College of Surgeons—Its Aims and Objects  
 GEORGE CRILE, M D , Cleveland  
 The March of Scientific Medicine. ALLEN B KANAVEL, M D , Chicago  
 The Approved Hospital—What It Means to You (Illustrated) MALCOLM T MACEachern, M D , Chicago  
 Prevention of Heart Disease. LEROY LONG, M D , Oklahoma City, Okla.  
 The Course and Curability of Cancer (Illustrated) BOWMAN C CROWELL, M D , Chicago  
 Maternal Care C JEFF MILLER, M D , New Orleans  
 The Conservation of the Health Welfare of Workers in Industry (Illustrated) FREDERIC A BESLEY, M D , Waukegan, Ill  
 Patients, Doctors, and Hospitals ROBERT JOLLY, Houston, Texas  
 Medical motion picture film

#### OAKLAND DAY

Wednesday, October 30, will be designated as Oakland Day. The clinical program for that day will be transferred to the hospitals in Alameda County on the east side of the bay, which includes Oakland, Berkeley and Alameda—a great metropolitan area with a population of over 500,000 people, having many splendid hospitals and the great University of California in Berkeley. No clinics will be scheduled in San Francisco hospitals on that day. Besides a wealth of clinical facilities, there are many points of interest which it will be the pleasure of the surgeons living in the district to show to the visiting Fellows and their families. The Oakland committee has arranged special transportation facilities for the visiting Fellows and their friends.

#### HOSPITAL CONFERENCE

The eighteenth annual hospital standardization conference will open with a session in the Gold Ballroom of the Fairmont Hotel at 9 30 on Monday morning at which addresses will be delivered by distinguished representatives of several organizations. At this session the annual report of the hospital standardization activities of the College for 1935, including the list of approved hospitals, will be presented.

Monday afternoon will be given over to a discussion of hospital problems from various aspects

in which administrators, surgeons and others will participate.

Tuesday morning will be devoted to a "panel" discussion of the hospital's obligation to its community and its part in the community life professionally and economically.

A joint session with the Association of Record Librarians will be held on Wednesday morning at which problems concerning hospital records are to be discussed.

Tuesday and Wednesday afternoons will be devoted to definitely planned departmental demonstrations in hospital administration in certain of the San Francisco hospitals. These demonstrations will show how various departments function, affording those present an excellent opportunity to see how other institutions carry on their activities.

Thursday will be Oakland Hospital Day and a program of demonstrations of special interest will be carried on in four of the major hospitals in Alameda County with the co-operation of the Oakland Hospital Council. Many new features and procedures in hospital management will be demonstrated.

Through the courtesy of Dr. D. W. Black, medical director of the Highland Hospital and director of Alameda County health activities, those who are interested in the Alameda plan for medical and hospital care will be given an opportunity to make an excursion through the county on Friday.

#### STATE AND PROVINCIAL COMMITTEES

A meeting of the State and Provincial Executive Committees with officers of the College has been called for 5 o'clock Monday afternoon in the Gray Room of the Fairmont Hotel. This meeting is called for the purpose of obtaining information on which may be based the itinerary of the College for its sectional meetings and the desirable grouping of the states and provinces.

#### ANNUAL MEETING

The annual meeting of the Fellows of the College will convene in the Gold Ballroom of the Fairmont Hotel at 1 30 o'clock Thursday afternoon. Reports by the officers and chairmen of the standing committees on the various activities of the College will be presented, followed by the election of officers.

#### SURGICAL FILM EXHIBITIONS

Throughout the week surgical motion picture films, both sound and silent, will be exhibited daily in the Red Room of the Fairmont Hotel. This showing of films, demonstrating clinical

features of interest, has met with popular acceptance in recent years. A number of new films are to be shown. Detailed programs will appear in the Daily Bulletin.

#### HEADQUARTERS—TECHNICAL EXHIBITION

Headquarters for the Congress will be established at the Fairmont and Mark Hopkins hotels. At the former the Terrace Ballroom and Foyer the Gold Ballroom and other large rooms on the main floor and on the terrace have been reserved for scientific sessions and conferences, registration and clinic ticket bureaus, bulletin boards, exhibits, executive offices etc.

The Technical Exhibition including the registration and clinic ticket bureaus, will be located in the ballroom and foyer on the terrace floor of the Fairmont Hotel. In these rooms will also be found the bulletin boards on which the daily clinical program will be posted each afternoon. The leading manufacturers of surgical instruments, X-ray apparatus, operating room lights, hospital apparatus and supplies, ligatures, dressings, pharmaceuticals and publishers of medical books will be represented in this exhibition.

#### A VACATION ON THE PACIFIC COAST

Many Fellows of the College and their guests, who will attend the Clinical Congress in San Francisco are planning to take advantage of the opportunity which naturally suggests itself to include a vacation and sight-seeing trip on the Pacific coast. All the railways are offering very low round-trip rates with liberal stopover privileges from all parts of the United States and Canada, with the added privilege of traveling to the coast by one route and returning by another thereby affording unusual opportunities for visiting many points of interest en route.

Few cities have so impressive a setting as San Francisco. The rugged hills upon which it is built, the Golden Gate, Mt. Tamalpais, the misty bay to the east, Oakland and Berkeley and the hills beyond, all contribute to its grandeur. It is a pleasing picture and the citizens of San Francisco have not been unmindful of it. Their parks and residence districts have a dignity and beauty in keeping with the scene about them.

Along the Pacific coast one will find much to claim his attention. First, there is the California Pacific International Exposition at San Diego—a World's Fair of magnitude with many important medical and other scientific exhibits—erected in Balboa Park, a tropical fairyland. The buildings, which are permanent structures, have their dignity and beauty enhanced by the gorgeous

setting. Sunday, November 3, has been designated as American College of Surgeons Day and a special program for that day is being prepared.

Los Angeles with its mountain background, its broad boulevards, its nearby beaches, its hospitality—and Hollywood—afford opportunities for entertainment and recreation.

Traveling south but a short distance from San Francisco, one enters the San Joaquin valley at Merced—the gateway to Yosemite National Park, where one views one of the most famous spectacles of nature. The valley occupies but eight square miles, but in this limited space are gathered more natural wonders than can be found in any other similar area in the world. It contains eight waterfalls, the lowest twice the height of Niagara, and the highest the equal of ten Niagara. There are meadows of deep grass and wild flowers, a rushing mountain river, forests and towering cliffs.

Del Monte and Pebble Beach, on the famous seventeen mile drive are but a short distance from San Francisco. Other nearby points of interest are Paso Robles with its almond groves, lovely Santa Barbara with its famous Old Mission, and a score of cities whose names are associated with the romantic Spanish period—a fairyland of natural and cultivated beauty.

To the north there are many cities to claim your attention. Vancouver in British Columbia, built up against mighty mountains with a primal forest almost at its environs, Seattle, the great shipping center of the northwest, with Puget Sound to the west and beyond it the white-capped Olympics in the distance the Cascade Mountains and looming to the southeast, Mt. Rainier held in special veneration by the Indians as the mountain that was God—no peak in the United States is so majestic. Portland, famous for its natural beauty—a literal tower of roses, the blue miracle of Crater Lake, Mt. Shasta and Lassen Peak, the only active volcano in the United States.

No matter what route one takes he will view a truly great and inspiring American scene—the thriving farm lands of the midwest, the noble stretches of prairie, the sublime mountain ranges of the Rockies, the grandeur of the desert, the towering forests of the far west, and then the blue Pacific.

This year one will travel in comfort and luxury undreamed of a short time ago. Whatever route one travels he will find his train air-conditioned. This single factor adds so much to the comfort and pleasure of a transcontinental journey that it definitely and certainly marks the beginning of a new era in transportation history.

RAILWAY FARES FROM VARIOUS CITIES TO  
SAN FRANCISCO AND RETURN

Low round-trip fares will be in effect from all points in the United States and Canada. Consult your local ticket agent as to exact fare. Summer tourist tickets are good going via one route and returning via the same or any other authorized route, with a final return limit of November 30.

	Round Trip Fare	Lower Berth One Way
Atlanta	\$100 75	\$21 25
Baltimore	120 75	24 00
Boston	132 80	25 88
Buffalo	109 55	21 38
Chicago	86 00	15 75
Cincinnati	97 00	19 50
Cleveland	101 35	19 50
Detroit	98 30	19 50
Duluth	86 00	17 75
Kansas City	72 00	13 25
Memphis	85 15	14 50
Minneapolis	86 00	15 75
Montreal	122 55	24 75
New York	126 90	24 75
New Orleans	85 15	14 00
Omaha	72 00	13 25
Philadelphia	122 85	24 00
Pittsburgh	107 10	20 25
Portland, Ore	29 70	5 50
St. Louis	81 50	15 00
St. Paul	86 00	15 75
Seattle	37 05	6 75
Toronto	108 15	21 38
Vancouver, B. C.	42 55	8 75
Washington	120 75	24 00
Winnipeg (via Portland)	86 00	18 75

## ADVANCE REGISTRATION

The hospitals and medical schools of San Francisco and Oakland afford accommodations for a large number of visiting surgeons, but to insure against overcrowding, attendance at the Congress will be limited to a number that can be comfortably accommodated at the clinics—the limit of attendance being based upon the result of a survey of the amphitheatres, operating rooms, and laboratories of the hospitals and medical schools to

determine their capacity for visitors. It is expected, therefore, that those surgeons who wish to attend the Congress will register in advance.

Admittance to all clinics and demonstrations will be controlled by means of special clinic tickets, which plan provides an efficient means for the distribution of the visiting surgeons among the several clinics and insures against overcrowding, as the number of tickets issued for any clinic will be limited to the capacity of the room in which that clinic will be given.

A registration fee of \$5.00 is required of each surgeon attending the annual Clinical Congress, such fees providing the funds with which to meet the expenses of the meeting. To each surgeon registering in advance a formal receipt for the registration fee is issued, which receipt is to be exchanged for a general admission card upon his registration at headquarters. This card, which is non-transferable, must be presented in order to secure clinic tickets and admission to the evening meetings.

## SAN FRANCISCO HOTELS AND THEIR RATES

In addition to the two headquarters hotels—the Fairmont and Mark Hopkins—there are a number of first-class hotels within short walking distance of headquarters providing ample hotel facilities at reasonable rates. The following hotels are recommended by the Committee.

	Minimum Rate with Bath	
	Single	Double
Bellevue, Geary and Taylor	\$3 00	\$4 00
Californian, Taylor and O'Tarrell	3 00	4 50
Clift, Geary and Taylor	3 50	5 00
El Cortez, Geary near Taylor	3 00	4 50
Fairmont, Mason and California	3 50	5 00
Gaylord, Jones near Geary	3 00	4 00
Mark Hopkins, Mason and California	3 50	5 00
Palace, Market and New Montgomery	3 50	5 00
Plaza, Post and Stockton	3 00	4 00
Sir Francis Drake, Powell and Sutter	3 50	5 00
Stewart, 353 Geary	2 50	4 00
St. Francis, Union Square	3 50	5 00

## OPHTHALMOLOGY AND OTOLARYNGOLOGY—SCIENTIFIC SESSIONS

*Tuesday 9:30—Gray Room, Fairmont Hotel*

JOSEPH L. MCCOOL, M.D. Chairman.

A New Iridocycloectomy Operation for Glaucoma CONRAD BERNER, M.D. New York.

Discussion opened by A. R. LEVINE, M.D. Los Angeles

The Management of Complications in the Operation for Senile Cataract. JOHN O. McREYNOLDS, M.D. Dallas, Texas.

Discussion opened by JOSEPH L. MCCOOL, M.D. San Francisco

Orbital Abscess DWIGHT C. OLCUTT, M.D., Chicago

Discussion opened by RAYMOND J. NUTTINS, M.D. Oakland

The Surgical Approach to the Nasal Accessory Sinuses. WILLIAM MITTNERBERGER, M.D. Cincinnati, Ohio

Discussion opened by EDWARD DEWALL, M.D. San Francisco

Motion Picture and Microscopical Studies of the Trans-antrum ethmo-sphenoidal Operation CHARLES E. FUTCH, M.D. Los Angeles

Discussion opened by GEORGE McCLEURE, M.D. Oakland.

*Thursday 9:30—Gray Room, Fairmont Hotel*

HARRINGTON B. GRAHAM, M.D. Chairman.

Brief Consideration of the History of the Development of Mastoidectomy ROBERT SCHNEIDERMAN, M.D. Chicago

Discussion opened by COL. A. E. SCHLANTZ.

Unique Symptoms and Effects of Sphenoidal Empyema. CHRISTIE H. BOWMAN, M.D. Los Angeles

Discussion opened by ROBERT C. MARTIN, M.D. San Francisco

Surgical Correction of Defects Due to Paralysis of the Muscles of the Eyes and of the Eyelids. ALFRED WYCKOFF, M.D. St. Louis.

Discussion opened by ROBERT C. O'CONNOR, M.D. Oakland.

The Relation of Orthoptics to the Surgical Treatment of Constant Strabismus. AVERY ORR PRAGER, M.D., Rochester, Minnesota

Discussion opened by HANS BARKAN, M.D. San Francisco.

*Friday 9:30—Gray Room, Fairmont Hotel*

JOSEPH L. MCCOOL, M.D. Chairman

Separated Retina Treatment with Galvano Caustery. CLIFFORD B. WALKER, M.D. Los Angeles.

Discussion opened by DOUGLASS K. FINCHILL, M.D. San Francisco

An Analysis of Five Hundred Intra-ocular Steel Operations. SIDNEY WALKER, JR. M.D., Chicago.

Discussion opened by OTTO BARKAN, M.D. San Francisco

Motion Picture Study of Laryngeal Pathology. F. E. LEEHUE, M.D. New Orleans

Discussion opened by WALLACE B. SMITH, M.D. San Francisco

Cancer of the Larynx. W. E. SAUER, M.D. St. Louis

Discussion opened by HARRINGTON B. GRAHAM, M.D. San Francisco

The Selection of Treatment for Malignancy of the Upper Respiratory Tract. FREDERICK A. FELL, M.D. Rochester, Minnesota

Discussion opened by REA E. ASHLEY, M.D. San Francisco

## PROGRAMS FOR EVENING MEETINGS

*Presidential Meeting—Monday, 8 15 p m—War Memorial Opera House*

Invocation

Address of Welcome HOWARD C NAFFZIGER, M D, San Francisco, Chairman of Committee on Arrangements

Introduction of Foreign Guests

Address of the Returning President The Conscience of the Surgeon ROBERT B GREENOUGH, M D, Boston

Inauguration of Officers President, DONALD C BALFOUR, M D, Rochester, Minn, First Vice-President, ARTHUR W ALLEN, M D, Boston, Second Vice-President, JOHN A GUNN, M D, Winnipeg

Treatment of Peptic Ulcer, Based on Physiological Principles ALTON OCHSNER, M D, New Orleans

Annual Oration on Surgery The American College of Surgeons—Past, Present and Future GEORGE CRILE, M D, Cleveland

*Tuesday, 8 15 p m—Auditorium, Veterans Building*

Symposium on Hypertension

The Medical Problem and Management of Essential Hypertension S MARX WHITE, M D, Minneapolis

Surgery in its Relation to Hypertension ALFRED W ADSON, M D, Rochester, Minn

Treatment of Hypertension by Splanchnicectomy MAX MINOR PEET, M D, Ann Arbor, Mich

*Wednesday, 8 15 p m—Auditorium, Veterans Building*

The Diagnosis and Treatment of Stone in the Common Duct ARTHUR W ALLEN, M D, Boston

Adrenal Cortical Tumors GEORGE F CAHILL, M D, New York

Some Aspects of Maternal Nutrition LEIGHTON C CONN, M D, Edmonton, Alta

Fracture Oration Fundamentals versus Gadgets in the Treatment of Fractures PAUL B MAGNUSON, M D, Chicago

*Thursday, 8 15 p m—Auditorium, Veterans Building*

Ischemic Contractures ARTHUR STEINDLER, M D, Iowa City, Iowa

Cerebral Injuries Due to External Trauma GEORGE W SWIFT, M D, Seattle

The Diagnosis of Endometrial Hyperplasia LUCIUS E BURCH, M D, Nashville, Tenn

The Iodine Relationships of Thyroid Disease GEORGE M CURTIS, M D, Columbus, Ohio

*Convocation—Friday, 8 15 p m—Scottish Rite Auditorium*

Invocation

Presentation of Candidates for Fellowship

Conferring of Fellowships The President

Conferring of Honorary Fellowships The President

President's Inaugural Address The Trend of Surgery DONALD C BALFOUR, M D, Rochester, Minn

Fellowship Address The Social Significance of Medicine ROBERT GORDON SPROUL, B S, LL D, Berkeley, Calif



*Monday, 2 00-5 00—Gold Ballroom, Fairmont Hotel*

BENJAMIN W. BLACK, M.D., Oakland, presiding  
 Application of the Principles of Hospital Standardization from the Viewpoints of  
 Hospital Trustee W. C. CRANDALL, La Jolla, Calif  
 Hospital Administrator PAUL H. FESLER, Chicago  
 Medical Staff Member JACOB F. HIGHSMITH, M.D., Fayetteville, N.C.  
 Clinical Pathologist ALVIN G. FORD, M.D., Pasadena, Calif  
 Radiologist EDWARD S. BLAINE, M.D., Los Angeles  
 Nurse SISTER MARY STEPHANIE, R.N., San Francisco  
 Dietitian LUCILE WAITE, San Leandro, Calif  
 Medical Social Worker MARGUERITE L. SPIERS, Oakland  
 Medical Educator ALEXANDER R. MUNROE, M.D., Edmonton, Alta  
 Economist DANIEL CROSBY, M.D., Oakland

*Tuesday, 9 30-12 30—Gold Ballroom, Fairmont Hotel*

ARTHUR M. CALVIN, St. Paul, presiding  
 Innovations in Hospital Equipment and Supplies from the Standpoint of Efficiency, Economy, and Service. G. W. OLSON, Los Angeles  
 The Institutional Care of Chronic and Convalescent Patients A. C. JENSEN, San Leandro, Calif  
 Panel Discussion Conducted by JOSEPH G. NORBY, Minneapolis  
 To Create Understanding—Public Relations FRANK J. WALTER, Denver  
 To Provide Adequate Service G. WAITE CURTIS, San Francisco  
 To Bring the Cost of Hospital Service Within Reach of the People Served R. E. HEERMAN, Los Angeles  
 To Provide Adequate Service to the Indigent Patient. J. V. BUCK, Spokane, Wash.  
 To Educate Nurses, Doctors, and Others Engaged in the Care of the Sick CAROLYN E. DAVIS, Portland, Ore.

*Tuesday, 2 00-5 00—St. Mary's Hospital*

Demonstrations and round table discussions dealing with methods of standardization and administration Conducted by SISTER MARY THOMASINE, Superintendent, and heads of departments  
 Business administration—equipment, personnel, accounting, reports hospital costs, methods for meeting present economic conditions  
 Organization and management of food service—control and responsibility, personnel, types of service, special diets  
 Pharmacy service—organization and management, physical requirements personnel, accounting  
 Adjunct departments—Organization and management of clinical laboratory, X-ray and physical therapy departments, technical service, routine examination, records and filing

*Tuesday, 8 00-10 00 p.m.—St. Mary's Hospital*

Round Table Conference—A discussion of every-day hospital problems as applied to the professional and economic aspects of hospital administration Conducted by ROBERT JOLLY, Houston, Texas

*Wednesday, 9 30-12 30—Gold Ballroom, Fairmont Hotel*

Joint Session with Association of Record Librarians of North America R. C. BUERKI, M.D., Madison, Wis., presiding  
 Securing, Supervising, and Using Medical Records MALCOLM T. MACEachern, M.D., Chicago  
 Discussion from the viewpoints of  
 Hospital Administrator THEODORE E. SWARTZ, M.D., Oakland.  
 Physician S. MARX WHITE, M.D., Minneapolis  
 Surgeon ALTON OCHSNER, M.D., New Orleans  
 Obstetrician D. G. TOLLEFSON, M.D., Los Angeles  
 Ophthalmologist and Otolaryngologist WILLIAM W. PEARSON, M.D., Des Moines, Iowa  
 Record Librarian RUTH M. SNIDER, Chicago  
 Group Studies Essential to Scientific Efficiency SISTER M. SERVATIA, R.N., Kansas City, Mo.

*Wednesday, 2 00-5 00—University of California Hospital*

Demonstration and round table conference on the organization and management of the medical records department Conducted by F. S. DURIE, Superintendent, and heads of departments.  
 Physical requirements, personnel, supervision, filing and cross-indexing records, uses of records, special problems, standard nomenclature.

*Wednesday, 2 00-5 00—San Francisco Hospital*

Demonstrations and round table conference on care of the obstetrical patient in the general hospital Conducted by LEON M. WILBOR, M.D., Superintendent, and heads of departments  
 Prenatal care, admission procedure, care of the patient in labor, delivery room technique, postpartum care, the isolated or septic patient, care of the newborn, follow-up and end results, review of morbidities and mortalities records Motion picture "Around the Clock with You and Your Baby"

## OAKLAND HOSPITAL DAY—THURSDAY

*10 00 a.m.—1 00 p.m.—Providence Hospital*

Demonstrations and round table conferences  
 Economies in hospital management. Staff of Providence Hospital.  
 Organization and management of the housekeeping department. Staff of Fairmont Hospital.  
 Organization and functioning of the social service department. Staffs of Alameda County and Berkeley General Hospitals.

*2 00-5 00—Samuel Merritt Hospital*

Demonstrations and round table conferences  
 Admission and discharge procedures Staffs of the Samuel Merritt and Peralta Hospitals  
 Organization and management of a central supply room Staff of Samuel Merritt Hospital.  
 Hospital formulary Staff of Peralta Hospital

*Friday, 10 a.m.*

Inspection of the emergency system of the Alameda County Hospital and tour of county institutions for study of the Alameda plan.



## COMMITTEE ON ARRANGEMENTS

## EXECUTIVE COMMITTEE

HOWARD C. NAFTZGER, Chairman THOMAS F. MULLIKEN, Secretary

LEROY C. ARNOTT  
HAROLD BRUNN  
EDMUND BUTLER  
WHITFIELD CRANE

CHARLES A. DUKES  
LEO ELSCHNER  
OLIVER D. HANLEY

FRANK HICKMAN  
EMILE F. HOLMAN  
ALFRED R. KILGORE

FRANK W. LYNCH  
JOSEPH L. MCCOOK  
ISAAC W. THOMAS

## SUB-COMMITTEES—SAN FRANCISCO

Clinical Program Committee (General Surgery)—ALFRED R. KILGORE, Chairman, EDMUND BUTLER, THOMAS F. MULLIKEN

Clinical Program Committee (Eye, Ear, Nose and Throat Surgery)—JOSEPH L. MCCOOK, Chairman, H. B. GRAHAM, WARREN D. HOWARD

Transportation Committee—EMILE F. HOLMAN, Chairman, G. D. DELFRAY, MILLARD R. OTTINGER

Public Meeting Committee—JACOB C. GEMER, Chairman, HAROLD M. BERNHEIM, EDGAR L. GILCHRIST, JACQUES P. GRAY, LEON M. WILSON

Golf Committee—LEON BROOKS, Chairman, HARRY ALDERSON, JAMES MORGAN, FRANK SHERIDAN

## HOSPITAL REPRESENTATIVES

## SAN FRANCISCO—GENERAL SURGERY

Franklin Hospital—ERVET GERRARD, LEON BROOKS  
French Hospital—AAA COLLINS, EDMUND MORGENTHAU  
Hospital for Children—LEON ARNOTT, ALMA FERNANDO

Lettermen General Hospital—ALFRED FRANK C. OBER  
Mary Help Hospital—ISAAC THOMAS, RAYMOND MILLS  
St. Elizabeth's Hospital—DUDLEY KERR

Mount Zion Hospital—HAROLD BRUNN, FRANKLIN HARRIS, ALBERT L. BROWN

St. Francis Hospital—JAMES O'CONNOR, CALVIN A. WALKER

St. Joseph Hospital—ALFRED R. KILGORE, J. MINTON MERRITT

St. Luke Hospital—G. D. DELFRAY, OTTO PRUDERER

St. Mary's Hospital—THOMAS E. BAILEY, PHILIP ARNOTT, DANIEL SOUTY

San Francisco Hospital—STANFORD UNIVERSITY SURGEON LEON ELSCHNER, C. MATHENY, L. ROBERTS, UNIVERSITY OF CALIFORNIA SURGEON HAROLD BRUNN, C. LAYMAN CALLAWAY, GEORGE K. RICHMOND

Shoreview Hospital for Crippled Children—ST. HANS

Southern Pacific General Hospital—WILLIAM W. ANDERSON, FRANK R. GORDON

Stanford University Hospitals—EMILE HOLMAN, PHILIP K. GILMAN, FREDERICK RICHMOND

Stanford University School of Medicine—LOREN CRANDALL, EMMETT RICHMOND

United States Marine Hospital—MARK J. WHITE, RICHARD L. WADSWORTH

University of California Hospitals—HOWARD C. NAFTZGER, H. CLAYTON BELL

University of California Medical School—LAWLEY FORTER, WALLACE TERRY

Veterans Administration Facility—P. E. JOHNSON, BENJAMIN H. HENNING, JOHN A. KENNEDY

## SAN FRANCISCO—SURGERY OF THE EYE, EAR, NOSE AND THROAT

French Hospital—EDWARD C. FARRER, RAYMOND, VICTOR D'ERICKS

Hospital for Children—GEORGE HOFORD

Lettermen General Hospital—A. E. SCHLASSER, H. C. MAWILL

Mary Help Hospital—FRANK HAY, J. W. CRAWFORD

Mount Zion Hospital—FRANK ROBERT, HERBERT COY

St. Francis Hospital—CHARLES A. BENTON, ALBERT KAWLINS

St. Joseph Hospital—ROY PARKINSON

St. Luke Hospital—ANDREW E. ECKHART, CHARLES B. TIER

St. Mary's Hospital—FRANCIS CONRAD, STANLEY BOERS

Southern Pacific General Hospital—WILSON SWETT

Stanford University Hospitals—EDWARD SEWELL, HARRIS BARKER, HARRINGTON B. GRAHAM, LOUIS MORGENTHAU

United States Marine Hospital—REA E. ASHLEY

University of California Hospitals—WALLACE TERRY, PETER C. CORNER, ROBERT C. MARTIN, C. ALLEN DICKET

Veterans Administration Facility—J. J. CAVITT, OTTO BARRA

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CHARLES A. DUKES, Vice Chairman

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## PRELIMINARY CLINICAL PROGRAM

GENERAL SURGERY, GYNECOLOGY, OBSTETRICS, ORTHOPEDICS, UROLOGY,  
PROCTOLOGY, SURGICAL PATHOLOGY, ETC

## CLINICS IN SAN FRANCISCO HOSPITALS

## SAN FRANCISCO HOSPITAL

*Monday—Stanford University Surgical Service*

## Amphitheater A—9

J W CLINE Cholecystectomy Discussion by H P HILL.  
C. MATHEWSON Splenectomy Discussion by E WAX-  
BURNL. ELOESSER Lobectomy, demonstration of cases, flap  
operation for tuberculous empyema, demonstration of  
cases. Discussion by P K BROWN

## Amphitheater B—9

E MORRISSEY Section and immediate suture of tibial  
nerve for ischemic pain, demonstration of cases,  
lantern slides and specimens.

E. B. TOWNE. Neurolysis

M R OTTINGER. Torek operation for undescended testicle.

C. MATHEWSON Open reduction for spiral fractures of the  
tibia.

## Amphitheater C—9

R. DUVN Conization of cervix

H VON GELDERN Perineal repair

A. V. PETTIT Vesicovaginal fistula.

K. SCHAUPP Hysterectomy

D DALLAS Vaginal hysterectomy

## Amphitheater A—2

D WOOD, H BARLAND, L. ELOESSER and G BARNETT  
Clinical pathological conference

E. BUTLER. Treatment of perforated peptic ulcers.

J W CLINE Volvulus of cecum.

M R OTTINGER. Injection treatment of rectal prolapse

W ROGERS Volkmann's contracture following burns.

## Nurses Home—2

A V PETTIT Treatment of pelvic inflammatory disease

R. DUNN Treatment of incomplete abortions

D DALLAS Operations in obstetrics.

G HARTMAN Pyuria and hematuria.

L. MICHELSON Obstruction of the neck of the bladder  
in the female.

## Ward B Solarium—2

J M MEHERIN Fractures of the tarsal scaphoid

C MATHEWSON Open reduction of spiral fractures of the  
tibiaD KING Functional anatomy and pathology of the shoul-  
der joint.

J W CLINE Internal derangement of radio humeral joint

N J HOWARD Fracture of the humerus, moving picture  
demonstration

## Tuberculosis Solarium—2

W L ROGERS Communicating empyemas

P PIERSON Influence of position on respiratory volume

T WIPER. Congenital cystic diseases of the lung

L. ELOESSER. Bronchial obstruction

*Tuesday—University of California Surgical Service*

## Amphitheater A—9

HAROLD BRUNN Gastric resection lobectomy, one stage

C M JOHNSON Perineal prostatectomy Discussion by  
FRANK HINMAN on prostatectomy versus transurethral  
resection

C L CALLANDER. Amputation of the thigh, a new method

## Amphitheater B—9

GEORGE K RHODES Gastro-enterostomy

WILLIAM G MOORE Hysterectomy for leiomyomata of the  
uterus.

F S FOOTE. Ventral hernioplasty, Gallie technique

ALSON R. KILGORE and OTTO H. PFLUEGER. Radical  
mastectomy

## Amphitheater C—9

F C BOST Repair of ruptured ligaments of knee joint.

W J COX. Reduction and fixation of fracture of hip

F C BOST, W J COX and V M DILLON. Reduction of  
several fractures.

## Amphitheater A—2

H E RUGGLES and J L. CARR. X-ray and clinical patho-  
logical conferenceHAROLD BRUNN Pulmonary abscess. Discussion of the  
bacteriology by C W WEISS

C L CALLANDER. A new amputation of thigh

H. M. BLACKFIELD Skin grafts

## Lecture Room, Nurses Home—2

Symposium The Newer Bacteriological Aspects of  
Surgical Infections

C W WEISS. Newer investigations on inflammation

A. HEIM Staphylococcal and streptococcal infections

A P KRUEGER. The principles of vaccine therapy

K F MEYER. Anaerobic infections—tetanus, gas bacillus,  
etc.

## Social Hall, Nurses Home—2

GEORGE K RHODES A study of 1000 cases of acute ap-  
pendicitis at the San Francisco Hospital.

C M JOHNSON Renal and perirenal infections

MARGARET SCHULZE Pelvic inflammatory disease

K O HALDEMAN Acute osteomyelitis

S H. MENTZER. Cholecystitis.

H. J. MCCORKLE. Perforated peptic ulcer

## Assembly Hall, Tuberculosis Wing—2

F G LINDE and K O HALDEMAN Compression fractures  
of the spine.

H W FLEMING Head injuries.

A. L. BROWN Traumatic injuries of the chest.

GEORGE K RHODES Traumatic injuries of abdomen.

F C BOST Fractures of the ankle with ligamentous  
tears.*Thursday—Stanford University Surgical Service*

## Amphitheater A—9

D KING Arthroplasty of hip joint.

W ROGERS Apicolysis paraffin fill, demonstrations Dis-  
cussion by CAROT BROWNL. ELOESSER. Thoracoplasty, demonstration of cases. Dis-  
cussion by P PIERSONT WIPER. Radical amputation of breast, demonstrations  
Discussion by H. GARLAND

## Amphitheater B—9

- J. M. MERRICK Gastric resection (Billroth I). Discussion by H. P. Hill.  
 E. BUTLER Proctoplasty. Discussion by GEORGE BAXTER and L. ELLERMAN.  
 E. BUTLER Resection of colon for congenital twist.  
 M. R. OTTENGREN Injection treatment of inguinal hernia.

## Amphitheater C—9

- O. HARTMAN Suprapubic prostatectomy.  
 R. G. CRAIG Nephrectomy.  
 L. RICHMOND Cystectomy and transplantation of ovary.  
 L. MCKENNA Plastic of kidney pelvis.

## Amphitheater A—9

- D. WOOD, H. GARDNER, L. ELLERMAN and O. BARTETT. Clinical pathological conference.  
 J. W. CLYDE Staphylococcus immunity tests.  
 EDWIN RICHMOND Occasional infections.  
 N. J. HOWARD Anaerobic gram stains.  
 E. BUTLER Roentgen and its diagnosis in injuries to the chest and abdomen.  
 C. MATHESON Lymphogranuloma inguinale benign strictures of rectum.

## Nurses Home—9

- R. G. CRAIG Urinary pails of obscure origin.  
 L. RICHMOND Fracture of femur.  
 O. HARTMAN Renal tuberculosis.  
 K. SCHAEFF Fibrosarcoma of uterus.  
 H. VON GUERBER Plastic operations of pelvis.

## Ward B Lecture—9

- C. MATHESON Demonstration of closed methods of treatment of fractures of the extremities.  
 D. KANE Treatment of sclerosing osteomyelitis.  
 J. M. MERRICK Spontaneous tendon rupture.  
 L. MCKENNA Tumors of the claudic spine as the cause of sciatica.

## Tuberculosis Seminar—9

- L. SEARY Ultimate results of thoracoplasty.  
 W. L. ROGERS, CAROL BROWN, P. FINEBERG and W. BOKS. Symposium on surgical treatment of pulmonary tuberculosis.  
 L. ELLERMAN Treatment of benign esophageal stricture.

## Friday—University of California Surgical Service

## Amphitheater A—9

- H. W. STEPHENS Thoracoplasty.  
 S. H. MERRICK Clinico-cystectomy.  
 HAROLD BROWN Resection of colon. resection of rectum.

## Amphitheater B—9

- GEORGE K. RICHMOND Chondrochondrothorax.  
 LEON GOLDMAN Thyroidectomy.  
 A. L. BROWN Nephroplasty.  
 L. P. FLAVEL Nephrectomy.

## Amphitheater C—9

- A. M. VOLLMER Uterine suspension.  
 MARGARET SCHULZ Vaginal repair.  
 H. M. BLACKBURN Repair of Dupuytren's contracture.  
 FRANK HILTON Utero-intestinal anastomosis, radical cystectomy.

## Operating Room N 3—9

- H. A. BROWN Neurolysis.  
 H. W. FINEBERG Repair of defect of skull.

## Ward B—9

- F. C. BOST, W. J. COX and V. M. DILLON Demonstration and reduction of fractures.

## Amphitheater A—9

- H. E. REYNOLDS and J. L. CARR X-ray and clinical pathological conference.  
 Fractures of the extremities with associated neuro-injuries.  
 F. C. BOST The orthopedic aspect. H. A. BROWN. The neurological aspect.  
 C. M. JONES Traumatic injuries of the genito-urinary tract.  
 W. J. COX Rupture of the lateral ligaments of the knee joint.

## Lecture Room, Nurses Home—9

- GEORGE K. RICHMOND Gas bacillus infections.  
 H. H. ALEXANDER, JR. Treatment of fractures of the os calcis.  
 HOWARD MORROW and HERMAN E. MILLER Fungal infections.  
 M. W. DREXLER and J. M. SERRAT Hepatic abscess, anemic and pyogenic.  
 GEORGE OGDEN Tuberculosis of the genito-urinary tract.

## Social Hall, Nurses Home—9—Cancer Symposium

- OTTO H. FRIEDLBERG Presentation of cases from the San Francisco Hospital Cancer Clinic.  
 ALBION R. KILBOUR Operation for cancer of breast, endometria, demonstration of cases.  
 LEON BRYAN Radiotherapy of breast cancer.  
 JAMES CARR and JONAS A. WILLIAMS Bone tumors.

## Assembly Hall, Tuberculosis Wing—9

- LEON GOLDMAN Hyperparathyroidism, parathyroid adenoma associated with generalized osteitis. Great cysts.  
 A. M. VOLLMER Sympathectomy in dysmenorrhea.  
 WALTER RICHMOND Traumatic injuries of tendons.  
 C. G. LYON Fractures of the metatarsals with cranial dislocation.

SAN FRANCISCO EMERGENCY HOSPITAL  
(Auditorium of Public Health Building)

## Tuesday—9

- JACOB C. GARDNER, Director of Public Health of San Francisco. Hospital care of the indigent.  
 EDWIN BUTLER Organization of the emergency hospital service of San Francisco.  
 GEORGE K. RICHMOND Acute operative work in the San Francisco Hospital. handling of the indigent.  
 JOHN M. SEARS Treatment of cyanide poisoning.  
 Inspection of Central Emergency Hospital and the ambulance.

## FRANKLIN HOSPITAL

## Tuesday—9

- G. W. FINEBERG and G. O'CONNOR Plastic surgery.  
 L. BROWN General surgery.  
 E. GARDNER Gastro-intestinal surgery.

## Thursday—9

- E. GARDNER Gastro-intestinal surgery.  
 L. BROWN General surgery.  
 G. HARTMAN and J. B. LEONARD Urologic surgery.  
 J. SALK, V. DILLON and O. MORROWORTH Orthopedic operations.

## UNIVERSITY OF CALIFORNIA HOSPITAL

## Monday—9

- R WARD—Room B Thyroidectomy  
 H BLACKFIELD—Room B Plastic surgery  
 W JONES, JR—Room C Operation for brachial neuritis  
 C ROSSON—Room C Ventral hernia  
 M WOLF—Room D Rectal surgery  
 M L MONTGOMERY—Room D Hernioplasty  
 F LYNCH—Room E Cervical repair, cystocele, rectocele, suspension, appendectomy  
 D MORTON—Room E Martin flap cervical resection, cystocele, rectocele  
 F BAKER—10 Demonstration of pool therapy  
 JOHN L MCGUINNESS—11 Demonstration on the use of the Pavaex unit  
 ROBERT S STONE—11 30 Demonstration of deep therapy plant

## Monday, 2—Toland Hall

- EUGENE S KILGORE Circulatory disease in differential diagnosis of acute abdomen  
 H. GLEN BELL and THEODORE ALTHAUSEN Pre-operative management of cholecystitis, operative mortality without routine glucose, with routine glucose therapy, with Rose Bengal and when necessary other routine tests as a pre-operative routine  
 FRANK LYNCH and ROBERT STONE Uterine cancer, X ray therapy radium therapy, follow up  
 HOMER WOOLSEY Carcinoma of stomach  
 ROBERTSON WARD Carcinoma of thyroid

## Monday, 2—Cole Hall

- HOWARD C NAFFZIGER and O W JONES, JR. Prevention and repair of skull defects.  
 FREDERIC FOOTE and J E CARR Experimental work on jaundiced patients, clinical application  
 HANS LISSER and L P PLAYER Presentation of a boy, aged 9 years, 4 years after the removal of an adrenocortical tumor causing sexual precocity  
 H BRODIE STEPHENS Subphrenic abscess.  
 Z E BOLIV Mixed tumors of the parotid gland

## Tuesday—9

- F HINMAN—Room B Perineal prostatectomy, nephrectomy  
 W I TERRY—Room C Substernal goiter  
 H G BELL—Room C Esophageal diverticula.  
 L C ABBOTT—Room D Sacral fusion with bone graft.  
 F LYNCH—Room E Proctidemia, vaginal hysterectomy and creation of new pelvic floor  
 D MORTON—Room E Hysterectomy for fibroids  
 N N EPSTEIN—10 Demonstration of pyro therapy  
 JOHN E MCGUINNESS—11 Demonstration on the use of the Pavaex unit.  
 ROBERT S STONE—11 30 Demonstration of deep therapy plant

## Tuesday, 2—Toland Hall

- WALLACE TERRY, H. H. SEARLS and E I BARTLETT Our conception of chronic diffuse thyroiditis  
 J B DE C M SAUNDERS The knee joint, functional anatomy and surgery  
 P CAMPICHE The present status of radiotherapy from the surgeon's standpoint.  
 CARL HOAG Reconstruction of the bile ducts  
 KARL SCHMIDT The bile salts

## Tuesday, 2—Cole Hall

- M L MONTGOMERY Acute intestinal obstruction  
 FRANK HINMAN Uretero-intestinal anastomosis  
 F I HARRIS and A C WHITE Injection treatment of hernia.  
 T F MCILLEN Antethoracic esophagoplasty  
 ROY ABBOTT The shoulder joint.

## Tuesday, 2—Room 437, Clinic Building

- Staff Cancer clinics FRANK LYNCH Gynecology E I BARTLETT Breast ROBERTSON WARD Thyroid. H. GLEN BELL Gastro intestinal C L CONNOR Pathology R. S STONE and H RUGGLES X ray

## Thursday—9

- F HINMAN—Room B Cystectomy, uretero-intestinal implantation  
 H C NAFFZIGER—Room C Laminectomy for spinal cord tumor  
 H H SEARLS—Room C Thyroidectomy  
 E I BARTLETT—Room D Radical mastectomy  
 W MOORE—Room E Hysterectomy for fibroids  
 M SCHULZE—Room E Cervical repair, cystocele, rectocele suspension  
 F BAKER—10 Demonstration of pool therapy  
 JOHN E MCGUINNESS—11 Demonstration on the use of the Pavaex unit  
 R S STONE—11 30 Demonstration of deep therapy plant

## Thursday, 2—Toland Hall

- W J KERR The heart in hyperthyroidism  
 H H SEARLS Thyroid adenomata with lowered or normal basal metabolic rate  
 DANIEL MORTON and ROBERT STONE. X ray pelvimetry, direct method  
 FRANCIS S SAYTH Calcium and phosphorus metabolism, clinical applications  
 E I BARTLETT Bone tumors

## Thursday, 2—Cole Hall

- W W WASHBURN Treatment of acute perforated ulcer  
 M L MONTGOMERY Peripheral vascular disease, sheets showing studies and care  
 O W JONES, JR. and HOWARD C NAFFZIGER. Low back pain and cord tumors  
 FRANK HINMAN and W K MURPHY Prostatism  
 DR. REINHARDT Vitamin C deficiency in arthritis.

## Thursday, 2—Room 437, Clinic Building

- Staff Cancer clinics M S WOLF Rectum L R. TAUSSIG Skin R MILLNER Lip and mouth E I BARTLETT Bone tumors C L CONNOR Pathology ROBERT S STONE and HOWARD RUGGLES X ray

## Friday—9

- H G BELL—Room B Cholecystectomy  
 H H SEARLS—Room B Gastro-enterostomy for pyloric obstruction  
 H C NAFFZIGER—Room C Splanchnic resection for essential hypertension  
 H BRUNN—Room C Lobectomy  
 L C ABBOTT—Room D Stabilization of foot, congenital torticollis  
 F LYNCH—Room E Removal of ovarian cyst and hysterectomy  
 D MORTON—Room E Cesarean section.  
 N N EPSTEIN—10 Demonstration of pyro therapy  
 JOHN E MCGUINNESS—11 Demonstration on the use of the Pavaex unit.  
 R S STONE—11 30 Demonstration of deep therapy plant.

*Friday 2—Tubal Hall*

- C. D. LEAKE and FRANK LYNN: Dyeing aside, new general anesthetic agent, its clinical use  
 M. S. WOOLY: Posterior resection of the rectum and its applied anatomy  
 H. GLEN BELL: Benign lesions of the small bowel  
 ROBERT ARND: Esophagography: clinical and experimental  
 F. C. BOET: Fracture of the saddle ligamentous tears

*Friday 3—Cole Hall*

- HAROLD BRUNY: Acute erysipelas  
 HIRSH MILLER: Coccydynia  
 KARL M. YER: The treatment of tetanus  
 ROBERT ARND and HOWARD C. NAFSTERER: Intracutaneous injections for intractable pain  
 JAMES W. MORGAN: The present conception of fistula and its management.

*Daily Demonstrations*

- C. L. CONYER: Demonstration in pathological museum  
 JOHN B. DE C. M. SANDERS and STAMFORD V. LARKIN: Exhibit on history of surgery

## STANFORD UNIVERSITY HOSPITAL

*Monday—3—Lane Hall*

- Symposium on Industrial and Orthopedic Surgery  
 ELMER RICHMOND: Knotty problems in industrial surgery  
 Traumatic carcinoma of breast ruptured heart, traumatic thrombosis of iliac and other large veins  
 A. L. FISHER: Sacro-lumbar lesions  
 DON KIRBY: The shoulder joint: its functional anatomy and pathology

*Symposium on Surgical Maggot Therapy*

- M. C. MERRON: Indications, technique and end results  
 EMERY W. SCHULTZ: Bacteriological studies with relation to bacteriophage  
 LEON O. PARKER: Mechanical and chemical aspects of larval therapy

*Monday—4—Varnes Auditorium**Symposium on Gastro-Intestinal Surgery*

- A. L. BLOOMFIELD: The physiology of the stomach with reference to surgical indications  
 GERTHER NAGEL: Indications for partial excision of the pyloric sphincter  
 EMERSON HOLMA: Important technical considerations in resections of the stomach for carcinoma  
 R. A. SCARBOROUGH: Developments in the surgical treatment of carcinoma of the rectum, with summary of 300 cases treated in the Stanford University clinic during the past twenty years  
 ELMER GRENDEL: Problems in surgery of the colon and rectum: Closure of artificial colostomy; prevention of anal sphincter treatment of diverticulosis

*The Etiology of Chronic Regional Enteritis*

- GERTHER NAGEL: Clinical observations  
 F. L. KIRCHER and M. E. MERRIS: Experimental observations  
 DON KIRBY: Multiple primary carcinomata complicating multiple polyps of colon  
 NELSON HOWARD: Anemic granuloma of large bowel

*Tuesday—5—Operating Suite*

- ELMER RICHMOND, P. K. GILM, S. STEPHEN BETHUNE, EMERSON HOLMA, E. B. TOWN, F. L. KIRCHER, GERTHER NAGEL, ELMER GRENDEL and R. A. SCARBOROUGH: General, industrial, proctological and neurological surgical operations.

*Tuesday—6—X-Ray Department*

- R. R. NEWELL and staff: Demonstration of supravoltage installation, demonstration of irradiation of cancer by divided dosage according to Coolard and Reppard, demonstration of radium application from multiple points to surface of body before up stitches on the irradiation treatment of cancer

*Tuesday—7—Lane Hall*

- LEONARD EMMER: Dysmenorrhea, causes and treatment: sterility diagnosis and treatment  
 C. F. FLETCHER, P. F. HORTON, and G. F. JONES: Endocrinological aspects of gynecology: Modern methods of diagnosis, blood and urine hormone tests, biopsy of the endometrium: hormone therapy  
 A. V. PARTIS: Results of hyperpyrexia in treatment of acute and chronic pelvic inflammatory disease  
 LEONARD EMMER: Radiation therapy of carcinoma of cervix, methods and end results

*Tuesday—8—Varnes Auditorium*

- PHILIP PETERSON: Carcinoma of lung obscuring inferior vena cava  
 EMERSON HOLMA: Technical improvements in partial resection thoracoplasty: resection of lower third of scapula  
 MARY E. MATHER: An experimental study of the effect of various pathological conditions upon the dual blood supply of the lungs: ligation of the pulmonary artery as therapeutic measure in pulmonary hemorrhage  
 EDGAR FORT: A simple apparatus for tidal and apneal stimulation and its application in the treatment of emphysema  
 DAVID A. WOOD and MARY E. MATHER: Clinical and experimental observations on the dual blood supply of the lungs in various pathological states

*Thursday—9—Operating Suite*

- LEONARD EMMER, H. A. STEPHENSON, C. F. FLETCHER, W. E. STEPHENS, GLEN CRANG, P. E. HORTON, A. D. DAVIS and STEPHEN BETHUNE: Gynecology: female urology: plastic and industrial surgery: operative clinic

*Thursday—10—X-Ray Department*

- R. R. NEWELL and staff: Demonstration of cinematogram: demonstration of pelvimetry: demonstration of hipoid injection of bronchi

*Thursday—11—Lane Hall*

- A. L. FISHER: Second type aneurysm complicating Colles' fracture: fracture of neck of femur: laceration of vulva and its treatment  
 DON KIRBY: Regeneration of the articular cartilage  
 LEON F. ASKE: Injection of joints with local anesthetic for diagnostic purposes with particles reference to the sacro-iliac joint  
 NELSON HOWARD: The treatment of epiphyseal fracture, dislocation at elbow  
 MERRILL MERRON: Unusual fractures of the spine  
 A. L. FISHER: The treatment of flat foot

*Thursday—12—Varnes Auditorium*

- Symposium on Surgical Diseases of the Breast  
 LEONARD EMMER: Experimental production of malignancy of breast  
 NELSON HOWARD: Etiology of cystic mastitis, experimental reproduction by hormone injection  
 ERIC LILJEVANDER: Treatment of inflammatory carcinoma of breast  
 F. L. KIRCHER: Demonstration of cleared specimens of breast tumors—benign and malignant

## Symposium on Surgical Diseases of the Blood Vessels

- F L REICHERT Treatment of circulatory disease of the extremities, interruption of the sympathetic nerves, passive vascular exercise
- NELSON HOWARD The varicose state. Results of operative and injection treatment of varicose veins
- EMILE HOLMAN The recognition and treatment of an arteriovenous aneurism
- F L REICHERT The "peripheral heart" to produce passive vascular exercise.

Thursday—3 30—Lane Library

- F L REICHERT History of Medicine Demonstration of medical incunabula

Friday—9—Operating Suite

- A L FISHER, DON KING, MERRILL MENSOR, LEON PARKER, J R DILLON, R L RIGDON, LLOYD REYNOLDS, LEO FLOESSER and EMILE HOLMAN Orthopedic, urologic and thoracic surgery

Friday—2—Lane Hall

- J R DILLON Treatment of chronic pyelitis and pyelonephritis. Technical improvements in surgical treatment of undescended testicle
- W E STEVENS Observations on pathological conditions of the urinary tract in women
- EDGAR POTH A new aseptic technique for uretero-enterostomy, mechanism of ascending infection of the urinary tract, experimental observations
- W E STEVENS and S P SMITH Scientific exhibit of interesting female urological conditions.

Friday—2—Nurses' Auditorium

- P K GILMAN Adenomata of the thyroid producing toxic symptoms without elevation of basal metabolic rate
- L G DOBSON End results of thyroidectomy for Graves' disease over a ten year period, demonstration of case showing cord paralysis coming on three weeks after thyroidectomy
- M E MATHE Results of thyroidectomy for Graves' disease in children
- L G DOBSON and L D HOWARD Clinical and laboratory studies in a case of hyperparathyroidism
- F L REICHERT Neuralgias of the cranial nerves, demonstration of patients lantern slides
- R A SCARBOROUGH and E J POTH Important mechanical factors in spinal anesthesia
- DAVID A. WOOD Exhibit of interesting endocrine tumors, operative and autopsy material

Friday—3 30—Surgical Laboratory

- F A FENDER Demonstration of apparatus for remote excitation of nervous system

## U S MARINE HOSPITAL

- ROBERT A JONES Excision of pilonidal sinus and rectal operations, cholecystectomy and autoplasty (Gillies tubular flap), Dupuytren's contracture
- E M TOWNSEND Inguinal hernioplasty using pedicle fascia strips, operation for sciatica (Heyman), arthrotomy of the knee with excision of internal semilunar cartilage, bunion operation (Peabody), phrenic neurectomy, transurethral resection of prostate.
- Staff Fracture clinic

## USS RELIEF

Tuesday

- HORACE R BOONE—9 Sacrococcygeal dermoids, caudal anesthesia in rectal surgery, traumatic surgery

## SOUTHERN PACIFIC GENERAL HOSPITAL

Tuesday—0

- WALTER B COFFEY and JOHN D HUMBER. Superior cervical sympathectomy for angina pectoris (motion picture film in natural colors), surgical treatment of angina pectoris, superior cervical sympathectomy
- C A WALKER. Operation for hydrocele with reference to total removal of sac.
- C P MATHE and T E GIBSON Transurethral prostatectomy
- EARL N GREENWOOD Cholecystectomy
- FRANK R GIRARD Inguinal hernia, ambulant treatment by injection
- O F NOLAN and T E GIBSON Suprapubic prostatectomy

Tuesday—2

- C A WALKER. Phrenicectomy for pleurocardiac adhesions, open reduction of fractures
- BERNARD KAUFMAN Phrenic nerve and precordial pain
- EARL N GREENWOOD Fractures of vertebrae, with particular emphasis on treatment, complications, end results of compressed fractures
- R EMMET ALLEN Complicating factors in the management of peptic ulcer
- PHILIP K BROWN Peptic ulcer, indications for surgical treatment
- C A THOMAS Surgical measures in pulmonary tuberculosis.
- W W WASHBURN Tumors of the parathyroid gland
- HENRY D BRUSCO Coccidioides granuloma, diagnosis and treatment
- W F SWETT and J C WILLIAMS Clinics and demonstration of cases.

Thursday—9

- G B O'CONNOR and G W PIERCE. Skin graft and pedicle graft in severe burn
- C A WALKER. Plating of fracture of tibia
- C P MATHE and T E GIBSON Hydronephrosis, plastic repair of, with case reports
- W W WASHBURN General surgical operations Gastro-enterostomy, thyroidectomy
- J A GUILFOIL Injection of hemorrhoids, demonstration
- FRANK R GIRARD Ambulant treatment of varicose ulcers, demonstration of cases.

Thursday—2

- C A WALKER and J E BOHM Mortality rate in operations for appendicitis.
- L B CROW Mediastinal effusions, roentgenological studies of, X ray demonstration of unusual fractures and results of treatment
- W F SWETT and J C WILLIAMS Clinics and demonstration of cases
- W T CUMMINS Pathological exhibits, gross and microscopic.
- W W WASHBURN Disabilities following fractures, factors influencing period of recovery, demonstration of cases.
- J E BOHM Dysinsulinism, hypoglycemia
- HENRY D BRUSCO Tularemia.
- BERNARD KAUFMAN Pathological lesions above the diaphragm simulating abdominal pathology
- J A GUILFOIL. Chronic appendicitis, results of operations for

## MOUNT ZION HOSPITAL

## Monday—

HAROLD BRUCE—Room 1. Radical mastectomy, cholecystectomy.  
FRANKLIN I. HARRIS—Room 2. Belts, repair of incisional hernia.

H. A. R. KREUTERMAN—Room 3. Nephrotomy, pyelotomy or nephrectomy.

RODMOND K. BOUTE, ABRAHAM BECKWITH, MORRIS H. SILVERBERG, ZACHARY CORLEW and SAMUEL R. SUTMAN—Room 5. Obstetrical clinic, chemical or section section.

A. LINCOLN BROWN—Room 5. Alcoholization of intestinal nerves for tuberculosis, Leotta method.

ALFRED ZONKE and DAVID A. SCHWOW—Room 4. Electrocoagulation of tumors of the rectum, hemorrhoidectomy, local infiltration.

EDWARD BOLLER, HERBERT SCHULTZ and STEPHEN LAZAR—Room 5. Demonstration of induction of anesthesia by avertin, evipal, gas and oxygen, apneal.

## Monday—

HAROLD BRUCE, A. LINCOLN BROWN, JOHN J. SACHS and HAROLD ROSENBLUTH. Symposium on surgery of the heart with particular reference to adhesive pericarditis.

ALFRED ZONKE and D. V. A. SCHWOW. Melanoma coli, demonstration of cases.

FRANKLIN I. HARRIS. Treatment of appendix stump with particular attention to the new revision method.

FRANKLIN I. HARRIS and ALFRED S. WHITE. Injection treatment of beriberi.

LOUIS C. JACOBS, ARTHUR EPPSTEIN, BENJAMIN STRAUSS and MAX POLER. Urological lesions of the female bladder: exhibition of rare pathological entities.

## Tuesday—

FRANKLIN I. HARRIS—Room 1. Tork operation for esophageal stricture, first and second stage procedures, subtotal gastrectomy for peptic ulcer, cholecystectomy.

LA. RENCE HOFFMAN—Room 3. Hysterectomy.  
FELIX I. PHARL—Room 3. Resection of inferior mesenteric plexus and superior hypogastric plexus for atonic lesion of bowel.

LEONARD D. PRINCE, ABRAHAM SIEGO and DAVID CHARNACK—Room 3. Reduction of fractured or colica, removal of semicircular cartilage of knee, orthopedic operations, correction of malformations, various procedures in hallux valgus.

ARTHUR EPPSTEIN—Room 4. Injection of vena deferens for chronic epididymitis.

BENJAMIN STRAUSS—Room 4. Hydrocele operation, plastic for phloema.

MAX POLER—Room 4. Cystoscopy.

GEORGE W. PIERCE—Room 4. Plastic surgery.  
EDWARD BOLLER, HERBERT SCHULTZ and STEPHEN LAZAR—Room 5. Demonstration of induction of anesthesia by avertin, evipal, gas and oxygen, apneal.

## Tuesday—

FRA. ELIN I. HARRIS. Chronic contracting enteritis (repeated attacks) demonstration of cases.

A. LINCOLN BROWN. Collapse therapy in the treatment of pulmonary tuberculosis, pneumococcus peritonitis, rupture of thoracic duct, demonstration of cases.

JOSEPH LAYMAN. Roentgenological demonstration. Local section of lung abscess, carcinoma of lung and tuberculosis.

ALFRED S. WHITE. Treatment of staphylococcus infection with streptolysin.

SAMUEL CORRY and FRANKLIN I. HARRIS. Treatment of undescended testicle by operation and glandular extracts.

FRANKLIN I. HARRIS. Surgery in acute cholecystitis.

G. Y. RYAN and GEORGE R. BARNES. Demonstration of intestinal pathological surgical specimens.

FRANKLIN I. HARRIS and G. Y. RYAN. Sarcoma of breast, pathology.

SAMUEL R. BERNER. Thoracic rupture of spleen with recovery lymphoblastoma (?) of neoplasm in two-year-old child.

## Tuesday—

HAROLD BRUCE—Room 1. Total thyroidectomy for carcinoma of thyroid, bilateral resection for carcinoma of bowels, thoracoplasty (thoracotomy or lobectomy).

A. LINCOLN BROWN—Room 3. Thoracoplasty, interruption of phrenic nerve, cholecystectomy.

FRA. ELIN I. HARRIS—Room 3. Hysterectomy for fibroid of uterus, interposition operation for prolapse repair of rectal sphincter following complete tear.

HARRY BLACKFIELD—Room 4. Plastic correction of congenitally protruding ears.

HARRY BLACKFIELD and FRANKLIN I. HARRIS—Room 4. Pilonus operation for ischioma and iliac side graft of chronic leg ulcer.

EDWARD BOLLER, HERBERT SCHULTZ and STEPHEN LAZAR—Room 5. Demonstration of induction of anesthesia by avertin, evipal, gas and oxygen, apneal.

## Tuesday—

HAROLD BRUCE. Pelvic appendicitis followed by carcinoma of rectum.

STAFF—Diseases of the peripheral arteries. Demonstration of thrombotic aneurysm, peripheral artery aneurysm block, cervical sympathetic aneurysm block, presentation of cases, results of treatment. Conditions amenable to surgery of the sympathetic nervous system. Cauphonomycin for hyperhidrosis, demonstration of case showing results.

EDWARD BOLLER. Removal of 1,000 cases of vertigo, hearing, experiences with evipal.

LEONARD D. PRINCE, ABRAHAM SIEGO, DAVID CHARNACK and GEORGE LANTIER. Fractures of os calcis, 40 cases, replacement of tibial shaft by fibula following osteomyelitis, treatment of burns, presentation of cases, clinical demonstrations of orthopedic cases.

CHARLES WEISS, JR., S. FELDSTEIN and D. V. LITVIN. Intraperitoneal vaccination: value of anesthetic, experimental pathology observed in monkeys.

## Friday—

LOUIS C. JACOBS, ARTHUR EPPSTEIN, MAX POLER and BENJAMIN STRAUSS—Room 4. Calculi of the urinary bladder, suprapubic prostatectomy, transurethral prostatectomy.

FELIX I. PHARL—Room 3. Anterior cervicothoracic ganglionectomy, extraperitoneal hepatic ganglionectomy.

FRANKLIN I. HARRIS, MORRIS J. GORDON and ALFRED S. WHITE—Room 5. Blood transfusion, citrate, Landis, Marx and Unger methods.

WILLIAM WALKER—Room 4. Appendectomy, laparoplasty.

EDWARD BOLLER, HERBERT SCHULTZ and STEPHEN LAZAR—Room 5. Demonstration of induction of anesthesia by avertin, evipal, gas and oxygen, apneal.

## Friday—

GEORGE W. PIERCE and HARRY BLACKFIELD. Plastic surgery. Demonstration and exhibition of postoperative plastic results.

- ERNST WOLFF Pyloric stenosis, diagnostic problems, twelve years experience with appendicitis in childhood, no mortality
- ANITA FAYERMAN Nonsurgical chronic abdominal pain in childhood (adolescence)
- ABRAHAM BERNSTEIN Obstetrical clinic Pre-eclamptic toxemia and treatment (motion picture) application of forceps and repair of perineum (motion picture), extraperitoneal cesarean section, presentation of cases and lantern slides.

*Daily—9 to 12 and 2 to 4*

- JOSEPH LEVITT Exhibit of diagrams and illustrative X rays—interlobar septa, lobes of the lung, study of the lower lobes, division into superior and inferior parts

## ST LUKE'S HOSPITAL

*Monday*

- OTTO H PFLUEGER—9 (Room B) Cancer of lip
- RUDOLPH L DRESEL, GEORGE J MCCLESNEY and W J COX—9 30 (Room A) Insertion of pin in fracture of the neck of femur
- ALANSON WEEKS and G D DELPRAT—10 30 (Room A) Chronic cholecystitis and cholelithiasis
- DUDLEY SMITH and J M MORGAN—10 30 (Room C) Carcinoma of the rectum

*Tuesday*

- G D DELPRAT—9 (Room A) Thoracoplasty
- J M MORGAN—9 30 (Room B) Pectenotomy, hemorrhoidectomy
- M VOLLMER—10 30 (Room A) Rubin's insufflation test
- W J COX—10 30 (Room B) Internal derangement of knee joint

*Tuesday—2*

- GEORGE J MCCLESNEY, W J COX and R L DRESEL. Fracture of neck of femur, treatment without external splinting
- W J COX Internal derangement of knee joint, rupture of ligaments treatment of fracture of femoral neck with Smith Petersen nails.
- DUDLEY SMITH and J W MORGAN Carcinoma of rectum
- ALANSON WEEKS and G D DELPRAT Thoracoplasty

*Thursday*

- PALL CASTELHUN—9 (Room B) Appendectomy, hernioplasty
- W G MOORE—9 (Room C) Supravaginal hysterectomy
- ALANSON WEEKS and G D DELPRAT—10 30 (Room A) Common duct stone

*Thursday—2*

- WILLIAM G MOORE. Endometriosis, fibromyomata of uterus
- A M VOLLMER. Rubin's insufflation test, trichomonas vaginitis
- ALANSON WEEKS and G D DELPRAT Common duct stone, hydatid disease of liver, needling subdeltoid bursa, use of glycerin alcohol in treatment of wounds and infections
- HOWARD W FLETCHER Subdural hematoma, cerebrospinal rhinorrhea relief of intractable pain cranial approach for orbital tumors craniocerebral injuries

*Friday*

- H FLETCHER—9 (Room A) Cerebrospinal rhinorrhea
- A H ROSENBERG—9 (Room B) Plastic correction duct.

## ST FRANCIS HOSPITAL

*Tuesday*

- LYOYD R. REYNOLDS and OSCAR NOLAN—9 Genito-urinary operative clinic, prostatectomy
- W W WASHBURN—10 General surgery thyroidectomy

*Tuesday—2*

- STERLING BUNNELL. Fracture of neck of femur, lantern slide demonstration.
- C A. FOGERTY X ray demonstration of lateral view of neck of femur
- CARL HOAG Reconstruction of common duct.
- RAY KISTLER. Review of some of surgical aspects of diaphragmatic hernia, presentation of cases.
- THOMAS STODDARD and EDWARD C BULL. Orthopedic clinic
- A. M. MOODY. Presentation of interesting pathological specimens.

*Thursday*

- GEORGE W PIERCE and GERALD B O'CONNOR—9 Plastic operations Reconstruction of face after burns, rib cartilage transplant to nose, removal of nasal hump, cleft palate, reconstruction surgery of hand

*Thursday—2*

- EDMUND J MORRISSEY Neurological clinic, shift of pineal as an aid in diagnosis of subdural hemorrhage.
- W B COFFEY and JOHN D HUMBER. Five year review of research on inoperable and hopeless malignant cases, the chemical and metabolic relation to the endocrine system and differentiation as to the selective causes of types.
- GEORGE W PIERCE and GERALD B O'CONNOR. Reconstruction surgery after burns lantern slide demonstration.
- OSCAR NOLAN Renal sympathectomy
- A. M. MOODY. Presentation of interesting pathological specimens.

## ST MARY'S HOSPITAL

*Monday—9*

- T GIBSON Nephrectomy
- W FALKNER. Bronchoscopic diagnosis of lung abscess

*Tuesday—9*

- D SOOY Surgical intervention for duodenal ulcer
- T F BAILLY Gastric surgery gastrectomy
- E. BUTLER Thyroidectomy, discussion during operation Clinical survey by RALPH REYNOLDS Pre operative throat examination by HARRINGTON B GRIMES
- E TOPHAM Inguinal hernia
- EDMUND MORRISSEY Sympathectomy for Raynaud's disease

*Thursday—9*

- R. VOELL. Gall bladder surgery cholecystectomy
- C P MATHIAS Nephropexy for nephropiosis
- G K KNODEN Emergency surgery
- P ARNOT Repair of extensive perineal tear, obstetrical surgery
- J LOEFTZHEIMER. Or treatment for delayed bony union.
- T J MULLEN Carcinoma of the esophagus

*Friday—9*

- J MCCARTHY Indus trial emergency cases



## HOSPITAL FOR CHILDREN

## Monday—

- MICHAEL E. EDWARDS and CARL L. HOWE (Room I) Thyroidectomy: thyroglossal duct cyst  
 GEORGE W. PRINCE and GERALD B. O'CONNOR (Room II) Plastic operations  
 LEROY C. ABBOTT and FREDERIC C. BOST (Room III) Spinal fusion for scoliosis  
 F. W. CALLESON (Room IV) General surgical operations

## Tuesday—

- H. H. M. REEL (Room I) Orthopedic operations  
 ALMA S. PETERSON (Room II) Gynecological operations  
 H. A. SYMPSON and D. A. DALLAS (Room III) Gynecological operations  
 SERRIN QUINN (Room IV) Cranio-vascular operations  
 PHILIP H. ARNOT (Room III) Gynecological operations  
 MARY E. MATTHEWS (Room III) Thoracoplasty  
 GEORGE W. PRINCE and GERALD B. O'CONNOR (Room IV) Plastic surgery  
 EUGEN K. WILLIAMS (Room IV) Gynecological operations  
 MICHAEL E. EDWARDS and CARL L. HOWE—so (Clerk Room). Hyperthyroidism in children: thyroglossal duct cysts, denervation of cases.

## Thursday—

- GERTRUDE F. JONES (Room I) Gynecological operations  
 LOUIS H. BUCK (Room I) Gynecological operations  
 GEORGE K. RICHIE (Room II) General surgical operations  
 A. R. KILLGORE (Room III) General surgical operations  
 JOHN SUTHERS (Room III) Gynecological operations  
 LEROY C. ABBOTT and FREDERIC C. BOST (Room III) Tibial leg lengthening  
 H. H. MARBLE (Room III) Orthopedic operations  
 FRANK H. ZERNWALD and S. BAKER PAGE (Room II) General surgical operations  
 ALBERT S. D. VEE (Room IV) Plastic surgery  
 MARY E. MATTHEWS—so (Clerk Room). Preliminary complications following intracranial operations, demonstration of cases and X rays.

## Friday—

- LEROY C. ABBOTT and FREDERIC C. BOST (Room I) Reconstruction for infantile paralysis  
 H. A. SYMPSON and D. A. DALLAS (Room II) Gynecological operations  
 PHILIP H. ARNOT (Room III) Gynecological operations  
 EUGEN K. WILLIAMS (Room III) General surgical operations  
 ALMA S. PETERSON (Room III) Gynecological operations  
 MARY E. MATTHEWS (Room IV) Operation for undescended testicle  
 A. R. KILLGORE (Room IV) General surgical operations

## MARY'S HELP HOSPITAL

## Monday—

- Staff Gynecological operations

## Monday—

- H. OT GILDER Pelvic reconstruction  
 DORLEY SMITH Racial fetids and hemorrhoidectomy involving picture demonstration  
 BEVELLE VERNON Separated placenta  
 ALICE H. SMITH Uterine bleeding  
 A. & M. SMITH Postoperative infections

## Tuesday—

- Staff Orthopedic operations

## Tuesday—

- M. MEYER and LOREN PARKER Skeletal traction in treatment of difficult fractures, osteomyelitis, its treatment with x-rays  
 LEE HARRIS Regeneration of peripheral nerves of hand after injury  
 C. C. McRAE Injuries to small bones of hand  
 R. J. MILLER, ZERA BOURN, R. KILL and I. W. THURVE Squamous and basal cell carcinoma of face and neck, diagnosis and treatment, pathology, radiation therapy, general discussion

## Thursday—

- Staff Cranio-vascular operations

## Thursday—

- ZERA BOURN Duodenal and tumor surgery  
 JOHN RICHARDS Mixed tumors of the parotid  
 FREDERICK CALVERT Carpal body tumors, splenectomy, indications and technique  
 W. B. FALMOR, JR. Treatment of chest injuries  
 W. A. CARROLL Ruptured kidney  
 M. V. STICK Ruptured aorta  
 R. J. MILLER Parathyroid injury during thyroidectomy

## Friday—

- Staff General surgical operations

## Friday—

- DODLEY SMITH Cancer of the rectum  
 FRAZ STILES Prevalent status of anorectal vein treatment

## VETERANS' ADMINISTRATION FACILITY

## Monday

- BEATRICE H. HARRISON—so Hemorrhoidectomy: Cuts, so also  
 F. L. E. JOHNSON—so Injection treatment of hemorrhoids, injection treatment of varicose veins  
 T. P. JONES—so The disability rating aspects of diseases of the bones and joints as the Veterans' Administration  
 S. B. M. FARLAND—so Unusual X ray films

## Tuesday

- F. L. E. JOHNSON—so Gastric surgery: biliary surgery  
 LEO ELLINGER—so Thoracic surgery

## Thursday

- P. S. JOHNSON—so Vagotomy: gastrectomy  
 BEATRICE H. HARRISON and JOE A. KENNEDY—so Direct surgical hernia: two cases  
 A. J. GREEN—so Outpatient treatment in Veterans' Administration facilities  
 EDWIN E. ZIEGLER Nutritional origin of cancer

## Friday

- PAUL E. JOHNSON—so Open reduction of fractures of femur closed reduction of fracture of tibia with Anderson apparatus  
 PAUL E. JOHNSON and BEATRICE H. HARRISON—so Demonstration of Bell orthopedic table and Rogers Anderson appliances for treatment of fractures

## FRENCH HOSPITAL

*Tuesday—9*

- W J HAWKINS, R F GRANT and C L COOLEY Gyne-  
cological operations  
ASA W COLLINS Radical hemorrhoidectomy by author's  
method

*Tuesday—2*

- E J MORRISSEY Diagnosis and treatment of subdural  
hemorrhages  
FRANK A. LOWE Fractures of humerus, surgical neck,  
shaft, supracondylar, moving picture demonstration.

*Thursday—9*

- FRANK A. LOWE Orthopedic operations  
ASA W COLLINS Pylorotomy, gastro-enterostomy

*Thursday—2*

- ASA W COLLINS Author's technique of partial resection of  
stomach, moving picture demonstration  
FRANK A. LOWE Internal derangement of knee joint.

*Friday—2*

- Symposium A preliminary report on investigations being  
carried out on San Quentin inmates to determine what  
health reactions follow the surgical removal of gingival  
and paradental infections (pyorrhea)

- PAUL J BOYENS Outline of plan and its purposes  
ALEXANDER G BARTLETT A general health survey of  
patients with paradental infections  
HILARIO G MARQUEZ Studies of the blood picture in  
paradental infections  
GEORGE F OVIFDO Paradental infections as related to  
prostatic infection  
L C GOBAR Summary of health changes in relation to  
paradentosis  
LEO STANLEY Discussion

## ST JOSEPH'S HOSPITAL

*Monday—9*

- CURTIS E SMITH General surgical operations  
A. SONNENBERG and B J ROHLFES General surgical  
operations  
T E GIBSON—Urological operations  
J W JONES General surgical operations  
A R. KILGORE General surgical operations

*Tuesday—9*

- RALPH SOTO-HALL and KEENE O HALDEMAN Orthopedic  
operations  
J M MEHERIN General surgical operations  
HANS VON GELDERN Gynecological operations  
T F GINSON Urological operations

*Thursday—9*

- CURTIS E SMITH General surgical operations  
T F GINSON Urological operations  
FRANK SHIELEY General surgical operations  
RALPH SOTO-HALL and KEENE O HALDEMAN Muscle  
and tendon injuries about the shoulder, demonstra-  
tion of cases.

*Friday—9*

- J. M MEHERIN General surgical operations  
FRANK SHIELEY General surgical operations  
EDWARD MORRISSEY Neurosurgical operations  
WESLEY E SCOTT General surgical operations  
A. R KILGORE General surgical operations  
HANS VON GELDERN General surgical operations

## LETTERMAN GENERAL HOSPITAL

*Monday—9*

- MAJ F L COLE Cauterization of cervix, perineorrhaphy,  
suspension of uterus, spinal anesthesia, two cases  
perineorrhaphy, hysterectomy, spinal anesthesia,  
inguinal hernia, spinal anesthesia, two cases, appen-  
dectomy, spinal anesthesia, two cases

*Tuesday—9*

- MAJ B S BURNET Bone graft in humerus, ether anes-  
thesia, open reduction of tibia, spinal anesthesia,  
excision cartilage of knee, spinal anesthesia  
MAJ H S BLESSE Electrical resection of prostate, spinal  
anesthesia, three cases

*Thursday—9*

- MAJ F L COLE Hemorrhoidectomy, spinal anesthesia  
three cases, colostomy for rectal carcinoma, spinal  
anesthesia, thoracotomy (empyema), gas oxygen  
anesthesia  
MAJ B S BURNETT Orthopedic operations  
MAJ H S BLESSE Electrical resection of prostate, spinal  
anesthesia, three cases

*Friday—9*

- MAJ P E DUGGINS Curettage, linear cauterization of  
cervix, perineorrhaphy, suspension of uterus spinal  
anesthesia, curettage and insertion of Carsten pessary  
for sterility, gas oxygen anesthesia.  
MAJ F L COLE Cesarean section, gas oxygen anesthe-  
sia, cholecystectomy, appendectomy, inguinal hernia,  
spinal anesthesia

## SHRINERS' HOSPITAL

*Monday*

- S L. HAAS and staff—9 Open reduction for congenital  
dislocation of hip joint, extra articular graft for tu-  
berculous hip, muscle transplantation

*Tuesday*

- S L. HAAS and staff—9 Transplantation of trapezius  
Sever operation and teres major transplantat on  
transplantation of biceps tendon

*Friday*

- S L. HAAS and staff—9 Lengthening of tibia and fibula  
Hibbs fusion of spine for scoliosis, longitudinal oste-  
otomy of tibia.

## CLINICS IN ALAMEDA COUNTY HOSPITALS—WEDNESDAY

## SAMUEL MERRITT HOSPITAL

- WALTER B. ALLEN—p (Room I) Reconstruction of skull defects, operation and demonstration of cases. Discussion by H. N. ROWELL.
- HENRY KNORR—p (Room II) Duodenal ulcer.
- FRANK R. MARTIN—p (Room III) Cholecystectomy. Discussion by A. A. ALFANDER.
- CHARLES A. DUKES and W. F. WILSON—p (Room IV) Chest surgery apicalysis—vs. pleurotomy demonstration of thirty cases by the method by pictures and cases. Medical presentation by HAROLD THOMAS.
- GEORGE G. REINHART—p (Room I) Nephrectomy. Discussion by F. D. GREER.
- MARIA L. ECKHART—p (Room III) Rectal surgery and presentation of cases.
- W. LARK MITCHELL—p (Room III) Pelvic tumor. Discussion by A. M. SMITH.
- HAROLD H. HITCHCOCK—p (Room IV) Orthopedic surgery. Discussion by CHARLES B. FOWLER.
- W. H. BAUMERT—p (Room V) X-ray demonstration and discussion of cases.
- ROBERT A. GUNN—p (Room V) Pathological exhibit, demonstration of frozen section technique and specimens.

## Dry Clinic, 2-3

- H. N. ROWELL, A. M. SMITH, W. H. STEINMANN, A. A. ALFANDER, W. S. KUTCH, H. GORDON MACLEAN, FLETCHER B. T. LOW, VERN O. ALDERMAN and HOMER ROBERTS—p Symposium on pre- and post-operative care. Management of surgical jaundice and stomach cases, diabetes in surgery, traumatic and postoperative pneumonia, cardiac and renal complications, postoperative psychosis, allergy in relation to abdominal surgery, discussion and demonstration of cases.

## BERKELEY GENERAL HOSPITAL

## Dry Clinic, 8-10

- FRANK D. WALSH. Cholecystitis, observations and comments on surgical treatment.
- CLAUDE H. CARPINE. Ectopic pregnancy recurring on same side.
- WILLIAM W. CHASE. Polycystic kidney nephroblastosis, prosthetic management.
- W. W. RUCK. Parathyroid disease, gross specimens and microprojections.
- R. G. V. NUTTS. X-ray demonstration and discussion.
- F. J. CARLSON. Other chondrodysplasia, case report clavicle dressing.

## CHILDREN'S HOSPITAL

- W. W. CHASE—p. Postmortem findings in the kidneys of children, lantern slide demonstration.
- CLIFFORD SWIFT and EDWIN M. T. RICE—p. Clinic on undescended testes. Demonstration of postoperative results, discussion of effect of testosterone S. demonstration of operation.

## ALAMEDA SANATORIUM

- J. ORAVITSKY—p (Room I) Hernioplasty under local anesthesia. preoperative.
- G. R. BURKE—p (Room II) Cholecystectomy.
- CHARLES HALL—p (Room I) Resection of stomach.

## ALAMEDA COUNTY HOSPITAL

- E. N. EWING—p (Room I) Total hysterectomy, subtotal hysterectomy, discussion of obstetrical service at Alameda County Hospital.
- WESTFIELD CRANE—p (Room II). Cancer of stomach. Discussion by FLETCHER B. TAYLOR.
- SCARVER EYERMAN—p (Room IV) Extraperitoneal the neoplasmy intraperitoneal pascuolysis clinic on placenta interruption and theorectomy. Discussion by CECILY BLISS.
- ALBERT M. MIRAGE, LLOYD KENDALL, JOHN A. D. CONNERT, T. I. WICKLEY and associates—p (Room V) Perineal proctostomy, suprapubic proctostomy, rectoscopic proctostomy operations, demonstration of cases, discussion.
- W. F. HOLCOMB—p (Room VI) Arthroplasty of hip.
- FRANK H. BOWLER and THORP LAMBERT—p (Room II) Cancer of rectum.
- CHARLES A. DUKES—p (Room I) Gynecological cancer, cholel; demonstration of intraperitoneal alcohol, hysterectomy and presentation of cases.
- H. W. HARRIS and DON D. WEAVER—p (Room II) Carcinoma of colon.
- L. B. BARLAND—p (Room VI) Arthroplasty of shoulder.
- LOUISE P. ADAMS—p (Room II) Carcinoma of breast.

## Dry Clinic, 2-4 30

- CHARLES A. DUKES and associates. Cancer cholel.
- HAROLD H. HITCHCOCK, N. A. CART and associates. Trepanning and orthopedic clinic, demonstration of Serrat head cast dryer, Bell table, plaster models, splints, etc.
- W. H. BAUMERT and C. B. BOWEN. X-ray exhibit and discussion.
- GERTRUDE MOORE. Pathological exhibit and conference.

## PERALTA HOSPITAL

- ERNO A. MAYERS and L. V. FORT—p (Room I) Cholel cystectomy. Discussion by JOHN H. DE C. M. SALTINER and A. P. KILBOE.
- FREDERICK M. LOCKER, JOHN W. SEIDER and J. SCOTT QUINLEY—p (Room II) Pericardial section.
- JOHN LOUIS LOWME and HAROLD P. MALONEY—p (Room I) Radical mastectomy.
- P. N. JACOBSON—p (Room III) Pericardectomy.
- HARRY J. THORP and C. J. LUNDSTROM—p (Room III) Carcinoma malignancies.

## Dry Clinic, 8-10

- Calcium dysfunction (including parathyroid hyperplasia).
- JOHN D. COATE. X-ray discussion.
- P. MICHAEL. Pathological consideration.

## EAST OAKLAND HOSPITAL

- DON D. WEAVER—p (Room I) Ulcer of stomach.
- H. J. THORP and C. J. LUNDSTROM—p (Room II) Carcinoma malignancies.
- O. R. EYER—p (Room III) Dry clinic. Surgery in the diabetic patient.
- CLARK RABIN—p (Room I) Prostate of uterus.
- HAROLD STEPHENS—p (Room II) Hysterectomy.
- R. S. V. NUTTS—p (Room III) Dry clinic. Vascuoplasia and position of viscera in healthy young adults, X-ray demonstration.
- ALEXANDER GRANT—p (Room II) Carcinoma of the rectosigmoid junction, Lacey technique.

ALTA BATES HOSPITAL

DEXTER RICHARDS—9 (Room I) Cholecystectomy  
DAVID HADDEN—9 (Room II) Perineorrhaphy  
J DWIGHT WILSON—10 30 (Room I) Ulcer of stomach  
THOMAS O LAKE—10 30 (Room II) Hysterectomy  
E SCHULZE HEALD—11 30 X-ray demonstration  
DAVID HADDEN Demonstration of anatomy of perineum

COWELL MEMORIAL HOSPITAL

HERBERT EVANS, ROBERT LEGGE, C A KOFOID and associates—9 Exhibit and discussion of latest advances in endocrinology, inspection of laboratories and hospital with special reference to the systematic medical care of university students, discussion of laboratory technique with particular reference to amebiasis

SURGERY OF THE EYE, EAR, NOSE, AND THROAT

CLINICS IN SAN FRANCISCO HOSPITALS

STANFORD UNIVERSITY HOSPITAL

*Monday—9*

L T HUNNICUTT Pathological studies  
HAROLD FLETCHER Presentation of cases

*Monday—2*

Staff Operative clinic.

*Tuesday—9*

DOHRMANN PISCHEL Demonstration of retinal detachment cases and moving picture of operation  
HANS BARKAN Demonstration of strabismus cases and moving picture of O'Connor cinch operation, demonstration of cataract cases with discussion of methods of operating  
AVERY HICKS Demonstration of cases of ocular tortu collis  
FRANK RODIN Cases of congenital and hereditary eye defects  
H B GRAHAM Congenital occlusion of ear with operative correction  
REAE ASHLEY Petrositis with spontaneous recovery, retropharyngeal abscess after tonsillectomy, general anesthesia  
HARVARD MCNAUGHT Complete stenosis of larynx, bilateral intrinsic carcinoma with laryngofissure

*Tuesday—2*

HANS BARKAN, DOHRMANN PISCHEL and staff Cataract, glaucoma and strabismus operations

*Thursday—9*

S V CHRISTERSON Retropharyngeal abscess, osteoma frontal sinus, syphilis of larynx.  
C B COWAN Pathological studies  
F D FELLOWS Acute osteomyelitis following intranasal antrotomy

*Thursday—2*

Staff Operative clinic.

*Friday—9*

J A BACHER Laryngofissure for bilateral paralysis, amyloid tumor of larynx, retrobulbar neuritis in child, relieved by fronto-ethmo-sphenoid operation, ionization in nasal conditions, acute mastoiditis  
A G RAWLINS Epidemic meningitis coincident with acute exacerbation of chronic, purulent otitis.  
R C MCNAUGHT Bilateral external fronto-ethmo-sphenoidectomy with pedicle flaps from septum.

*Friday—2*

HANS BARKAN, DOHRMANN PISCHEL and staff. Cataract, glaucoma and strabismus operations

UNIVERSITY OF CALIFORNIA HOSPITAL

*Monday—9*

W B SMITH—Room F Otorhinolaryngology, operative clinic.

*Tuesday—9*

W B SMITH—Room L Otorhinolaryngology, operative clinic.

*Tuesday—2*

WARREN D HORNER, JOSEPH W CRAWFORD C ALLEN DICKEY and DAVID O HARRINGTON Ophthalmological operations  
WALLACE B SMITH, LOUIS MORRISON and EDITH STOKER Otolaryngological operations  
JOSEPH W CRAWFORD Tuberculosis of eye  
C ALLEN DICKEY Surgery of the vertical muscles  
DAVID O HARRINGTON Contact glasses, practical demonstration  
R C MARTIN and STERLING BUNNELL Injuries and repair of the facial nerve

*Thursday—9*

W B SMITH—Room F Otorhinolaryngology operative clinic

*Thursday—2*

WARREN D HORNER, JOSEPH W CRAWFORD, C ALLEN DICKEY and DAVID O HARRINGTON Ophthalmological operations.  
WALLACE B SMITH, LOUIS MORRISON and EDITH STOKER. Otolaryngological operations.  
JOHN SAUNDERS Regional anatomy of the mastoid and pathways of infection of the intracranium.  
HOWARD C NAFFZIGER Brain abscess arising from middle ear and mastoid infections.  
WALLACE SMITH Phlebitis and thrombosis following middle ear and mastoid infections

*Friday—9*

W B SMITH—Room F Otorhinolaryngology, operative clinic

*Friday—2*

JOSEPH W CRAWFORD The eye in diabetes.  
C ALLEN DICKEY Ptosis, modification of Motais  
DAVID O HARRINGTON Tobacco amblyopia and its treatment.

ST LUKE'S HOSPITAL

*Tuesday and Thursday*

JOSEPH L MCCOOL, C ALLEN DICKEY, A E EDGERTON and CHARLES BATES—9 Ophthalmological clinic.

## SAN FRANCISCO HOSPITAL

Tuesday—

WALLACE B. SMITH, L. F. MORRISON, EDWIN M. STOKES and A. H. RICE: Radical mastoidectomy radical antrum, labyrinthectomy.  
W. D. HORTON, J. W. CRAWFORD and C. A. DICKET: Ophthalmology

Dry Clinic

WALTER D. HORTON: External laryngotomy history, uses, techniques, advantages.  
C. ALLEN DICKET and JOSEPH W. CRAWFORD: Society procedures in cataract operations, glaucoma, intra-ocular injections, use of lid retractors, pre-operative medication.  
WALTER D. HORTON, C. ALLEN DICKET and JOSEPH W. CRAWFORD: The use of synthetic epinephrine bicarbonate in ocular therapeutics.  
ALFRED RAVENHILL: Outcomes of the various, more common foreign bodies in the lungs, course of recovery from acute pneumonia, extensive osteomyelitis of the frontal bone.  
HARRINGTON B. GRAHAM: Foreign bodies in the lungs, stenosis of the esophagus, cancer of the larynx.  
HARRINGTON B. GRAHAM and J. M. WOLFFSON: Extensive abscess of the mediastinum.  
REA E. ASHCLEY: Treatment of tuberculosis of the larynx.

Thursday—

ROBERT INVER, W. E. BOULEY and FRED BOULEY: Shortening of the eyeball for detached retina, cataract extraction and strabismus.

Thursday—

WALTER D. HORTON, C. ALLEN DICKET and JOSEPH W. CRAWFORD: Cataract extraction strabismus operations, ptosis and glaucoma.

## SOUTHERN PACIFIC GENERAL HOSPITAL

Tuesday

WILLIAM F. SWIFT—y: Nose extraction of cataract.

Thursday

WILLIAM F. SWIFT—y: Retinal detachment.  
WILLIAM F. SWIFT and JOHN C. WILLIAMS—y: Chorea and demonstration of cases.

## LETTERMAN GENERAL HOSPITAL

Tuesday

A. E. SCHLAEGER and HERBERT PERK: Tonsillectomy, adenoidectomy, general anesthesia, eye surgery, general anesthesia, strabismus correction, O'Connor arch shortening and junction recession.

## VETERANS' ADMINISTRATION FACILITY

Tuesday

J. J. CAYDICE: Otolaryngological and ophthalmological operations.  
Staff: Bronchoscopic examinations.

## ST. MARY'S HOSPITAL

Thursday—

FRANCIS CONWAY, STANLEY H. KEE and FRANK HAMP: Treatment of posterior anastomosis, blood dyscrasias in relation to the ear, nose and throat, treatment of bilateral abductor paralysis.  
FRANK HAMP: Radical antrum.

## MOUNT ZION HOSPITAL

Tuesday—

HENRY J. CONY, EDWARD LEMERT and JOHN SEATT: Tonsil operations, local and general anesthesia, dissection, bladder anastomosis.

Wednesday—

HENRY J. CONY, EDW. ED. LEMERT and JOHN SEATT: Symposium on mastoidectomy.  
GEORGE B. LACHMAN: Treatment of cerebral worms.  
CHARLES WELLS: Recently developed concepts in immunology and bacteriology of otitis to the ophthalmologist.  
FRANK RUDIN: Treatment of acute otitis media.  
G. V. RICE: Pathological demonstration of various eye conditions.

Thursday—

Staff: Nasal operations, Subconjunctival reaction, electro-magnetism of instillations, nose surgery.

Days to be announced

FRANK H. RUDIN and GEORGE B. LACHMAN—y: Ophthalmological operations, Cataract, strabismus, plastic eye cyclids.

## HOSPITAL FOR CHILDREN

Thursday—

GEORGE N. HORTON and AVERY M. HICKS: Extraction of congenital cataract, muscle operations, O'Connor arch shortening for temple exotropia, temple exotropia, vertical deviations, muscle transplants for external rectus palsy, superior rectus for palsy of the superior oblique (Jackson's technique). Alveolar operation for congenital ptosis, Two Minkler operations for correction of nasolacrimal duct (with DR. MARTIN and HORTON).

Dry Clinic

GEORGE N. HORTON and AVERY M. HICKS: Technique for the determination of the hydrogen ion concentration of tears, the significance of pH of tears in ocular symptoms and treatment, indications for and results of orthoptic training: relation of vertical imbalance of extra-ocular muscles to gastric symptoms, posture, temperament and aptitude for school work and education, congenital muscle palsy, motion picture demonstration of O'Connor technique for heterotropia and heterotropia.

## MARY'S HELP HOSPITAL

Friday

FRANK HAMP—: Treatment of bilateral abductor paralysis of the larynx.  
HARRISON PARKMAN—: Differential diagnosis of external strab.

## FRENCH HOSPITAL

Tuesday—

R. C. FAIRBANKS, VICTOR D'ENROLES and C. B. CONWAY: Ophthalmological and otolaryngological operations.

## CLINICS IN OAKLAND HOSPITALS—WEDNESDAY

## PROVIDENCE HOSPITAL

A J HOWELL—9 Reconstruction of nose  
 RODERIC O CONNOR—9 Muscle shortening, cataract,  
 Curran operation  
 GEORGE McCLOURE and NELSON KEELER—9 Esopha-  
 goscopy and bronchoscopy  
 RANDOLPH SHARPSTEEN—9 Motais' operation  
 ROY NELSON—9 Esophagoscopy and bronchoscopy  
 BRUCE STEPHENS, JR.—10 Cataract operation  
 FRANK BAXTER—10 Ear, nose and throat operations  
 MILTON H SHUTES—10 Ear, nose and throat operations  
 ALEXANDER GALBRAITH—10 Ear, nose and throat opera-  
 tions.

W A MAGRATH—11 Eye operations  
 ALVIN P WOLD—11 Eye surgery  
 F C KRACAW—11 Ear, nose and throat surgery  
 R J NUTTING—12 Eye operations.  
 P T LEFTWICH—12 Ear, nose and throat surgery  
 FRANCIS SHOOK—12 Ear, nose and throat surgery  
 SYDNEY N PARKINSON—12 Treatment of acute and sub  
 acute paranasal sinus infections, lantern slide and  
 motion picture demonstration

*Dry Clinic, 2-4 30*

Staff —Discussion of operative procedures, demonstration  
 of cases, lantern and motion picture demonstration



# SURGERY, GYNECOLOGY AND OBSTETRICS

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## THE EXPERIMENTAL PRODUCTION OF CHOLESTEROSIS OF THE GALL BLADDER

WITH OBSERVATIONS ON THE CHOLESTEROL ABSORPTIVE PROPERTIES OF THE GALL-BLADDER WALL<sup>1</sup>

LOUIS M. ROUSSELOT, M.D., AND LOUIS BAUMAN, M.D., PH.D. NEW YORK, NEW YORK

THE appearance of lipid deposits in the wall of the gall bladder early attracted the attention of pathological anatomists. Thus Virchow in 1857 commented on the presence of lipid material in the epithelium of many of the gall bladders obtained at necropsy. Naunyn in his treatise on gall stones states that he found an increased concentration of cholesterol in the gall bladder bile of gall stone cases. He believed this was due to secretory activity of the gall-bladder epithelium. Years later Aschoff presented the opposite concept namely that cholesterol could be absorbed by the gall-bladder wall. Subsequently many publications have appeared to support one or the other belief.

The similarity of the histological structure of the gall bladder and intestine and their derivation from a common anlage lead many to speculate as to possible similar functions. Thus Policard, Sweet, Halpert, and Mentzer (19) thought that the gall-bladder mucosa possessed absorptive properties. Sweet, in fact, believed that few if any of the bile constituents left the gall bladder by way of the cystic duct. After studying similar histological material other observers have arrived at exactly the opposite conclusion, thus Chauffard, Gosset and Lichtwitz believed that the gall-bladder mucosa exercised a secretory function as far as cholesterol was concerned.

Sir Berkeley Moynihan first drew attention to the clinical-pathological entity which was later named the "strawberry gall bladder" by MacCarthy, and more aptly cholesterosis of the gall bladder by Mentzer (19). Using microchemical reactions, differential stains and the polarizing microscope, Policard (27), Boyd and Illingworth concluded that the epithelial deposits of lipid material in cholesterosis cases consisted principally of the ester of cholesterol, and that this followed absorption of cholesterol from the bile.

In spite of the many opinions, direct experimental proof of the cholesterol function of the gall bladder is meager. A review of the various approaches to the problem is of interest.

Aschoff, after ligating the cystic duct of dogs and injecting neutral fats and cholesterol dissolved in olive oil into the gall bladder, observed lipid deposits in the epithelial cells and concluded that this was due to absorption. Apparently he failed to consider that the gall-bladder epithelium of normal dogs may show varying amounts of lipid material, for Chauffard, in a series of 6 normal animals found lipid in 3, while Boyd (4) found it present in every one of 12 animals. In our own group of 7 controls, small to large deposits were demonstrable in 6.

Tornoumi, after injecting normal bile and bile fortified by the addition of cholesterol

<sup>1</sup>From the Departments of Surgery of the Presbyterian Hospital and the College of Physicians and Surgeons, Columbia University.



TABLE I—THE CHANGE IN CHOLESTEROL CONTENT OF SOLUTIONS SUBJECTED TO GALL BLADDER ACTIVITY

Dog No	Cholesterol injected mgm	Cholesterol recovered mgm	Pct. lost	Length of time in gall bladder hours
107	26 26		60 64	12½ 14
111	23 26		60 20	20½ 14
109	26 23	27	60	6 12
	24 24	14	26 1	12
112	26 26	24	+	5 14
106	60 60	60 20	20	24 14
107	22	21	100	2½ 23½
26	22 22	20 20	25	24 24

into the gall bladder reported absorption in 3 experiments, and secretion in 2 infected cases. He concluded that, while cholesterol is normally absorbed the process may be reversed in the presence of infection.

Illingworth injected bile to which cholesterol ester was added (a substance rarely found in human bile—Pierce, 15) into the gall bladder of cats and found a loss of about 50 per cent. He reports only two experiments of this type.

Elman and Taussig and Elman and Graham injected bile into the gall bladder of the dog with the cystic duct ligated. They found an increase in the cholesterol content after a period of from 2 to 16 days. In these experiments, the partitioning ligature method of Rous and McMaster was used. Samples of gall bladder and hepatic bile were analyzed. The cholesterol content of the gall-bladder fraction was higher than could be accounted for by concentration, hence they concluded that the gall bladder secreted cholesterol.

Blaisdell and Chandler after producing hypercholesteremia in rabbits and dogs, found microscopic evidence of cholesterol in the epithelium and submucosa of the gall bladder. This occurred only when the cystic duct was patent and represented one of many foci that were present in various organs. The gall

TABLE II—THE CHOLESTEROL CONTENT OF THE GALL BLADDER WALL OF DOGS INJECTED WITH A SOLUTION OF CHOLESTEROL IN BILE SALT

Number	Total cholesterol per cent*	Total cholesterol per cent*
1	26	97
5	26	47
1287	65	40
2280	30	15
2304	55	14
336	15	27
Average	40	66
Total cholesterol content		66

\*The values are expressed in terms of dry gall bladder substance.

bladder infiltration was explained on the basis of absorption.

Recently Patey working along similar lines produced a hypercholesteremia in rabbits. After inducing inflammatory changes in the gall-bladder wall he was able to demonstrate microscopic deposits of lipid in the gall-bladder mucosa in only 7 of 10 experiments. In contrast to the previous authors he interpreted the process as one of secretion.

Ravdin (28, 29) and his colleagues were unable to demonstrate absorption or secretion of cholesterol by the normal gall bladder of the dog. The experiments of Willie and Doubilet led them to conclude that normally cholesterol passes through the gall-bladder mucosa into the bile, but the process may be reversed depending on the relative concentration of the cholesterol in the blood and the gall-bladder bile. Doulet believed that the normal gall-bladder mucosa secreted cholesterol in negligible amounts.

Cholelithiasis and cholesterosis, and the frequent association of the two conditions is a problem that has interested us for some time. Mentzer (30, 2) at the Mayo Clinic, found stones in 60 per cent of the cases of cholesterosis in his surgical material and only 2.4 per cent in a study of necropsy specimens. In an examination of the surgical material of the Presbyterian Hospital we have found a much higher incidence in that 75 per cent of the cases of cholesterosis also had gall stones. Because of this frequent association, a causal relationship between the two conditions has been suggested. Thus Gosset (12) Boyd (3)

TABLE III—THE CHOLESTROL CONTENT OF THE GALL-BLADDER WALL OF NORMAL DOGS

Number	Free cholesterol Per cent	Ester cholesterol Per cent
1	23	0
2	12	0
3	37	21
4	56	06
5	0	55
336	97	28
550	1 50	1 05
551	1 53	64
Average	66	35
Total cholesterol content		1 01

TABLE IV—THE CHOLESTEROL CONTENT OF THE GALL-BLADDER WALL OF DOGS INJECTED WITH SALINE SOLUTION

Number	Free cholesterol Per cent	Ester cholesterol Per cent
12320	98	66
12332	85	35
12369	1 13	26
12386	1 10	18
Average	1 01	36
Total cholesterol content		1 37

TABLE V—THE CHOLESTEROL CONTENT OF THE GALL-BLADDER WALL OF DOGS INJECTED WITH BILE SALT SOLUTION

Number	Free cholesterol Per cent	Ester cholesterol Per cent
12420	1 07	0
12448	1 10	36
Average	1 08	18
Total cholesterol content		1 26

and Elman (9) agreed that the later stage of cholesterosis may lead to gall-stone formation though they disagreed as to the origin of the cholesterol found in the wall

# EXPERIMENTAL

An attempt to study the fate of cholesterol in the gall bladder was made along the following lines

*Method* Large healthy dogs were operated upon under ether anesthesia, and the biliary tract was exposed. Anomalous bile ducts were carefully sought for in the region of gall bladder and cystic duct and these were ligated if they entered either of these structures. The gall bladder was then catheterized after the method used by Ravdin (28). A soft No. 8 F rubber catheter was passed through a small incision in the common duct just below the cystic duct. The catheter was then continued up the cystic duct into the gall bladder. The central hepatic duct was ligated above the cystic and below the entrance of the catheter. This system did not leak, did not occlude the rich vascular and lymphatic drainage along the cystic duct, and allowed sufficient bile to enter the duodenum so as to interfere as little as possible with digestion. The gall bladder was then irrigated with normal saline until a clear return was obtained. Saline was then injected and the capacity of the viscus determined. The saline solution was left in about 5 hours. This allowed sufficient time for the animal to recover from the immediate effects of the anesthesia and gave us another clue as to the presence of accessory ducts not detected at operation. At the end of 5 hours the gall bladder was again irrigated with saline

and the experimental solution instilled. After 24 hours the gall-bladder contents were aspirated, the viscus irrigated with saline and all the washings added to the sample. A second injection of the experimental solution was then made and again removed after a 24 hour stay in the gall bladder. Duplicate samples of the injection fluid were taken at each injection for check analyses of cholesterol by the Windhaus gravimetric method. The cholesterol solution contained 0.2 per cent of cholesterol dissolved in a 4 per cent solution of conjugated bile salts. This is the first time, we believe that a true solution of this type was used rather than bile or a colloidal suspension of cholesterol.

# DISCUSSION OF CHEMICAL FINDINGS

As was expected, there was a constant decrease in the volume of the injected fluid. In 5 of the animals an average loss of about 50 per cent in cholesterol took place (Table I). In 2 cases, 12 199 and 12 336, the loss was so small as to be within the realm of experimental error. Animal No. 12,252 showed a gain in the first 24 hours and a loss in the second 24 hours.

After the last sample of fluid was obtained the animal was immediately sacrificed and an autopsy was performed. The gall bladder was then removed, sections taken from the am-



Fig. 2. Photograph of normal gall bladder of the dog (actual size) b, Photograph of gall bladder of experimental animal. Note: bute opaque swollen with in ampullary region. These changes are less marked toward the fundus.

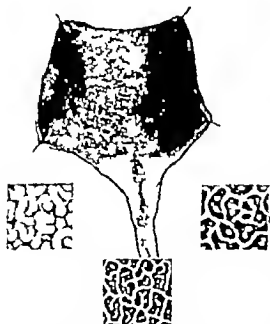


Fig. 3. Drawing illustrating marked gross changes in the region of the ampulla and cystic duct. A less intense change is seen toward the fundus. a, Appearance of white opaque lipid-laden villi in the ampullary region as seen with isopropyl alcohol glass. The intervening crypts are almost obliterated. b, Section from the margins of Figure 3 showing almost normal appearing translucent villi with deep intervening crypts. (Same magnification as Figure 3a.) Drawing by A. L. Enberg. c, Appearance of villi in the light-colored area in the fundus. The change is less marked. (Same magnification as Figure 3a.)



Fig. 4. Same as Figure 3, only enlarged one and two-third times. Area from ampulla shown. The heavily lipid-lipid containing villi stand out prominently.

pulla and fundus and the remainder was used for quantitative determination of cholesterol and cholesterol ester. Comparable analyses were also done (1) on the gall bladders of normal dogs (2) on dogs that were subjected to the same operative procedure but in which only saline solution was injected, and a third group that were injected with bile salt solution alone.

In the walls of human strawberry gall bladders we have consistently found an increase in the cholesterol and particularly in cholesterol ester as compared with normal gall bladders or those the seat of choleliths. In the animals injected with cholesterol solution the average total cholesterol content was 2.06 per cent (Table II) as compared with 1.01 per cent (Table III) in normal untreated dogs, 1.37 per cent (Table IV) in the saline controls, and 1.26 per cent (Table V) in the bile salt controls.

It is interesting to note the increment in the cholesterol ester content of our experimental animals as compared with the normal and the controls. If we take the average cholesterol ester content of the three control series as 0.3 per cent, the increase in the cholesterol ester of the injected animals was 100 per cent (0.66 per cent); this we think is far more than could reasonably be expected from any slight evaporation of cholesterol rich serum due to an inflammatory reaction. Wells (34) has shown

that inflammatory exudates are rich in cholesterol

The cholesterol and cholesterol esters in the wall of the gall bladder was determined by adaptation of the methods proposed by Fev and Gardner and Gainesborough as follows — A small amount of gall bladder was dried to constant weight at 110 degrees to determine the solid matter. The remainder was dissolved in 2 per cent sodium hydroxide by heating for 3 or 4 hours on the water bath. The alkaline solution was exhaustively extracted with ether. The residue which remained after evaporation of the ether was taken up in alcohol and free cholesterol precipitated with digitonin and weighed. The filtrate containing the cholesterol esters was saponified with 4 per cent sodium ethylate for 8 hours, then extracted and the cholesterol determined as above.

#### DISCUSSION OF PATHOLOGICAL FINDINGS

The gall bladder into which the cholesterol solutions had been injected showed a constant gross pathological change which was not observed in any of the controls. The villi of the mucosa appeared swollen, yellowish-white, and opaque in contrast to the thin greenish translucent villi of the normal organ (Figs 1 and 2). This change was constantly present in the region of the ampulla but a patchy distribution and a diffuse process was observed in several cases (Fig 3). In some instances the villi were so broad that they encroached on one another and the intervening crypts were difficult to see (Fig 3a). These changes were best seen with a hand lens and are well illustrated in Figures 2 and 3a and 3b. The lesions produced in these experimental animals is strikingly similar to the illustrations presented by Whipple in his clinical article on lipid gall bladder.

The histological preparations were taken from the ampulla and fundus, and stained with hematoxylin-eosin and Scharlach R. In some cases, unstained sections were studied with the polarizing microscope. The experimental animals all showed the brilliant red deposits of lipid in the epithelial cells, and occasionally in the stroma. Anisotropic lipid was also present in these same cells. Although

heavy deposits of visible lipid occurred in all our experimental animals we placed little significance on these findings inasmuch as 6 of 7 of our normal unoperated upon controls showed varying amounts of microscopically visible lipid. In all our experimental animals the sections showed mild inflammatory changes in the submucosa. We agree with Illingworth that all the cholesterol in the gall-bladder wall may not be demonstrable by staining methods. (Free cholesterol itself does not take the fat stain.) He felt that cholesterol may be bound up with other lipoids in such a manner as to render it unrecognizable by staining reactions or physical properties and that its passage through the gall bladder wall may likewise be obscured.

#### SUMMARY

When solutions of cholesterol in the concentrations mentioned are placed in the gall bladder of a dog there is a consistent loss of the lipid averaging about 50 per cent in 24 hours.

A gross pathological lesion was produced in every experiment that closely resembled the human picture of cholesterosis.

An increment in the cholesterol ester content of the gall-bladder wall was obtained. This is consistent with findings in the human specimens.

No apparent increase in the free cholesterol content of the gall-bladder wall could be demonstrated.

This evidence, under the conditions previously outlined, suggests the absorption of cholesterol by the gall-bladder mucosa.

We wish to express our indebtedness to Dr. A. P. Stout for his kind assistance in the study of the pathological material. Acknowledgment is also made of the technical assistance of Margaret Hamlin, M.A., and Albrecht Sauerman, Ph.D.

#### BIBLIOGRAPHY

1. ASCHOFF, L. Muenchen med. Wchnschr., 1906, 53, 1847.
2. BLAISDELL, F. E., and CHANDLER, L. R. Am J M Sc., 1927, 174, 492.
3. BOYD, WILLIAM. Brit J Surg., 1922, 10, 337.
4. Idem. Canadian M Ass J., 1922, 12, 689.
5. CHALFEARD, A., LAROCHE, G., and GRICAUT, A. Compt rend Soc. de biol., 1913, 74, 1005.
6. DOSTAL, HEDIVA, and GORF. Proc. Soc. Exper Biol & Med., 1932, 29, 541.
7. ELMAN, R., and GRAHAM, C. Arch. Surg., 1932, 27, 14.

- 8 ELMAH, R. and T. DEBOS, J. B. *Proc. Soc. Exper. Biol. & Med.* 93, 28, 666, 668, 670
- 9 IDEM, J. *Exper. Med.* 93, 54, 773
- 10 FICK, J. *Biochem. Ztschr.* 930, 64, 8
- 11 GARDNER, J. A. and GAINSBOROUGH, H. *Biochem. J.* 937, 30
- 12 GOSSET, M., LOEW, G. and MAGNAN, J. *Compt. rend. Soc. de biol.* 930, 83, 307
- 13 IDEM, *Bull. et mém. Soc. de Par.* 93, 47, 30
- 14 HALPER, B. *Med. Klin.* 924, N. 3, 408
- 15 IDAM, N. 5
- 16 ILLINGWORTH, C. F. W. *Brit. J. Surg.* 929, 2, 203
- 17 LACHETATZ, L. *Ergebn. d. inn. Med. Kinderh.* 92, 3, 56
- 18 MACCARTHY, W. C. *Ann. Surg.* 90, 5, 65
- 19 MENDER, S. H. *Am. J. Path.* 925, 383
- 20 IDEM, *Surg. Gynec. & Obst.* 926, 42, 783
- 21 IDEM, *J. Am. M. Ass.* 923, 90, 607
- 22 MOYERMAN, B. G. A. *Ann. Surg.* 909, 30, 265
- 23 NAUNYN, W. A. *Treatise on Cholelithiasis*. New Sydenham Society in English ed. 896
- 24 PERRY, D. H. *Brit. J. Surg.* 934, 2, 378
- 25 PEARCE, S. J. S. *Arch. f. klin. Med.* 92, 26, 337
- 26 POLICARD, A. *Compt. rend. Soc. de biol.* 924, 76, 318
- 27 IDAM, 5, 8
- 28 RAYMON, JOHNSON, et al. *Am. J. Physiol.* 932, 90, 638
- 29 RINGAL, JOHNSON, and RAYMON, J. *Exper. Med.* 932, 50
- 30 ROUS, P. and M. MARTIN, P. D. *J. Exper. Med.* 9, 44, 47
- 31 S. KAT, J. *Internat. Clin.* 924, 57
- 32 THORNTON, K. *Beitr. path. Anat. allg. Path.* 924, 7, 456
- 33 VINCOW, R. *Arch. f. path. Anat.* 837, 574
- 34 WELLS, H. O. *Chemical Pathology* 5th ed. pp. 300, 300 Philadelphia W. B. Saunders Co. 925
- 35 WHITFIELD, A. O. *Wheeler Loose Leaf Living Surgery* Vol. 5 p. 460
- 36 WILKIE, A. and DOUGLASS, Arch. Surg. 911, 26

## THE INTERVERTEBRAL DISC

EMBRYOLOGY, ANATOMY, PHYSIOLOGY, AND PATHOLOGY<sup>1</sup>

ROBERT J JOPLIN, A B, M D, BOSTON, MASSACHUSETTS  
 Assistant in the Department of Orthopedic Surgery of the Harvard Medical School  
 From the Orthopedic and Pathological Departments of the Children's Hospital, Boston

IN attempting to analyze the etiological factors which make up the clinical orthopedic problem of this day and age, the spine plays a major role. Schmorl is responsible for making popular a particular portion of the vertebral column which previously had been allowed to go by almost unrecognized. Instead of the main supporting structure of our head and trunk being regarded simply as a column of blocks separated by little fibrocartilaginous discs, an analysis of the component parts of each block and disc has changed our semi-flexible column into a very complex structure subject to a wide range of changes with far reaching results.

As a skeletal organ the spine is unique in structure and function. The joints differ from other joints of the body, as pointed out by Beadle, because not only do they possess flexion and rotation, but their broad surfaces bear the greater part of the burden of the spine and upon them fall the various stresses and strains of functional activity as well as the physical shocks leading to mechanical injury. The maximum effect is upon the structures between the bodies of the vertebrae. Instead of the usual joint cavity, there is a highly elastic and fluid tissue mass, the nucleus pulposus, a clear understanding of which requires a review of the embryological development.

## EMBRYOLOGY

Von Luschka, in 1858, was the first to report changes in the notochord leading to the formation of the intervertebral disc. Keys and Compere have summarized the more recent findings. In the human embryo, slightly over 2 millimeters long, a ridge of entodermal cells appears in the mid-sagittal plane and later separates as the notochord, in turn is surrounded by mesenchymal cells from the sclerotomes.

The aorta then sends in parallel branches which divide these cells into groups or seg-

ments (Fig 1). The cells which are nearest the blood vessels appear to receive more nourishment and differentiate more rapidly, that is those just above the artery and those just below rapidly grow to form the primordia or genesis of the vertebral bodies. Whereas the cells farther away from the blood vessels remain relatively unchanged as the primordia of the intervertebral discs.

In a mid-sagittal section at this stage, the notochord appears as a tube passing through segmented masses of cells. In the lighter segment, where the cells have grown by adding more cytoplasm, the notochord appears to be compressed in such a way that its cells are beginning to be extruded above and below toward the intervertebral spaces (Fig 2). Finally only a mucoid streak remains through the vertebral bodies. Still later, the cells of the intervertebral region differentiate into an elongated fibroblastic type, arrange themselves along a vertical axis and become attached above and below to the vertebral bodies.

In a 10 weeks old embryo which is approximately 5 centimeters in length, the vertebral bodies are cartilaginous and possess ossification centers. The notochord material may henceforth be regarded as the nucleus pulposus and its surrounding fibrocartilage envelope as the annulus fibrosus or annulus lamellosus. As the age of the embryo advances, the mucoid content of the nucleus pulposus is increased.

## ANATOMY

A cross section of an intervertebral disc from an infant 5 months of age reveals a gradual change from the hyaline cartilage type of cell at the periphery to an almost complete disappearance of cellular structure within the interior. First, there is the gradual loss of chondromucoid substance which leaves iso-

<sup>1</sup>Read at the Children's Hospital, Boston, October 19, 1933, as a part of the clinical program of the orthopedic section of the American College of Surgeons.

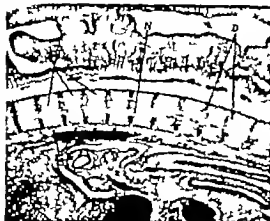


Fig. 2 (14th to 15th thoracic vertebral region in an embryo 14 millimeters long, 6 weeks old) The notochord, *N*, is seen passing through the segmented masses of cells. Above is dorsal, below is ventral. Here cross sectioned blood vessels, *B*, may be seen opposite the lighter areas, *V*, which form the vertebral bodies, the darker areas, *D*, form the discs.

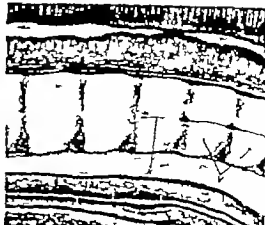


Fig. 3 (5th to 6th cervical region in an embryo 1 millimeter long, 8 weeks old) The notochord, *N*, is narrower in the vertebral body regions, *V*, but more globular between them.

lated cartilage cells in their lacunae. Farther toward the interior the lacunar membrane is present but the cells become pyknotic and finally disappear entirely leaving only a fibrillar network. In the central portion of the disc, a small clump of cells may be found (Fig. 3) but they appear a little denser and resemble prechondral tissue: these are the last remaining notochord cells. The mucoid content of the nucleus pulposus is markedly in-

creased as the infant gets older. It becomes increasingly difficult to identify notochord cells with the advance in age though remnants of these cells have been reported in the adult. About the time the child starts to walk the growth of the disc is chiefly by proliferation of the fibrous element.

The adult disc shows microscopically a very loose and translucent network of fine fibrous strands which run an irregular wavy course. In the meshes lie a profusion of long connective tissue cells and numerous cartilage cells.

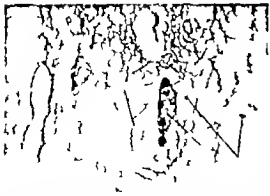


Fig. 4 High power photomicrograph of a section of the intervertebral disc from an infant 5 months old showing the web like fibrillar network, *F*, few scattered cartilage cells, *C*, and a small clump of last appears to be the last remnants of the notochord cells, *N*.

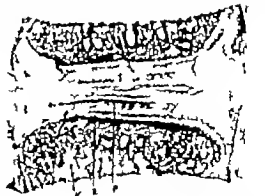


Fig. 5 Photomicrograph of sagittally cut sections showing two bony vertebral bodies, *V*, enchondral bone formation, *E*, and the cartilaginous plates, *P*, which overlap somewhat anteriorly.

A cross section of an 8 months old infant's spine reveals by gross examination, the enchondral bone formation which proceeds from the center of the vertebra toward the cartilaginous plates, between which lies the disc (Fig 4) At the periphery, the cartilage plate overlaps the anterior and lateral borders of the osseous vertebra and forms an incomplete bony ring, the so-called "epiphyseal ring," which Schmorl calls the "rim ledge" Enchondral bone formation ceases and fusion between the rim ledge and body of the vertebra occur simultaneously when full growth is reached

On the adult vertebral body (Fig 5) the rim ledge measures about 2 to 3 millimeters in width and stands 1.5 to 2 millimeters in height above the surface of the vertebra as a firm, compact, smooth, bony ring which partly encloses the disc anteriorly and laterally but not posteriorly Into this compact bone the annulus fibrosus fibers are firmly attached as Sharpey fibers The remaining central surface of the vertebra is composed of a perforated plate which is merely the bare exposed end of spongy bone which impinges immediately on the cartilaginous plate of the intervertebral disc It may be mentioned here that these perforations may be enlarged or easily broken through by protrusions of disc tissue

The intervertebral disc when fully developed is a most complex and highly specialized organ It consists of three parts the cartilaginous plates enclosing it above and below, next



Fig 6 Photograph of a mid sagittal section of the vertebral column of a 4 weeks old infant, no fixation has been used The nuclei pulposi, N, can be seen extruded clearly above the surfaces of the vertebral bodies

the surrounding annulus lamellosus which encloses the innermost structure, the nucleus pulposus

The blood supply of the intervertebral disc is not clearly understood Bohmig and Ubermuth are reported to have demonstrated in embryos that 3 vessels enter the intervertebral disc from above and 3 from below, these vessels retrogress during the course of life until, at the end of growth the intervertebral disc is completely without vessels

#### PHYSIOLOGY

It is the nucleus pulposus which plays the most outstanding rôle in the pathological changes which are to be described When the spine of a young person (Fig 6) especially of a child, is sawed through in a sagittal plane, the nucleus swells strongly forward as a white, translucent cushion which must have been under considerable pressure

In position, the nucleus pulposus is situated always rather more posteriorly than centrally



Fig 5 Photograph of an old macerated vertebra which shows a normal center with the rim ledge, R, complete on the front and lateral sides but deficient posteriorly, the mid portion of the picture reveals the perforated plate of spongy bone S

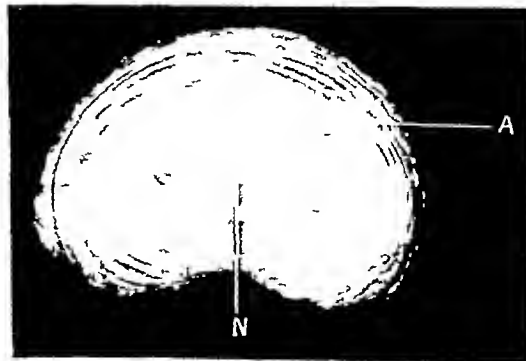


Fig 7 Photograph of a normal disc removed at autopsy from a woman 30 years old The horizontally cut section shows the annulus fibers, A, clearly as strong bands the more homogeneous central portion contains the gelatinous nucleus pulposus, N



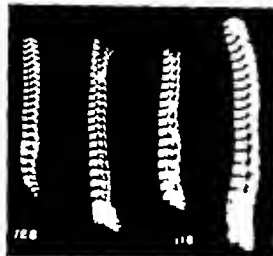


Fig 8. Lateral roentgenograms of 4 spinal columns. The one on the extreme left is from a 7 months old embryo which has discs almost as high as the vertebral bodies. The second is from an infant 1 week old, the third is from an infant 3 weeks old and the last is from an infant of 3 months. The discs appear relatively lower as the age increases. The notches in the anterior edges of the vertebral bodies are for the entrance of blood vessels.

This varies in different spinal segments. It is farther forward in the upper dorsal region.

There is no definite line of demarcation separating the nucleus pulposus from the annulus fibrosus though on horizontal section the two may be clearly distinguished. The annulus, of course, gives the permanent form and size to the disc as well as being the part where most of the strength and tenacity has its seat. Toward the periphery its concentric folds stand out as stout glistening bands which encircle the whole disc surface (Fig 7). The number of these folds vary. In the lumbar spine there are 10 to 12 exceedingly stout ones. In the lower dorsal region, only 6 lamellae may be counted. It is important to note that not only is there a lack of support from the bony rim ledge posteriorly but the concentric folds of fibrous tissue also are fewer and thinner here where they are attached to the posterior longitudinal spinal ligament. This ligament is a much weaker structure than the one anterior.

The nucleus pulposus may be considered subject to the laws of fluids, that is, it is incompressible and confined to its normal shape



Fig 9. Anteroposterior and lateral roentgenograms of spinal column of girl 13 1/2 years old who died of primary liver tumor producing marked osteoporosis. Here the discs, D, are much thicker than the vertebral bodies, V.

and position by the strong bands of the annulus fibrosus. It has been compared to a system of hydrostatic ball bearings. Any compression of the disc must result, therefore, in changing the shape of the annulus fibrosus. The amount of compression which it will stand depends upon the elasticity and strength of this structure.

As regards the stability of this semi-fluid supporting structure, it is important to note that there is a strategic point of weakness posteriorly as compared with the anterior edge of the disc. Not only is there a lack of restraint from the bony rim ledge posteriorly but the concentric folds of fibrous tissue are fewer and thinner here. Also the posterior longitudinal ligament is weaker than its anterior counterpart.



Fig 10

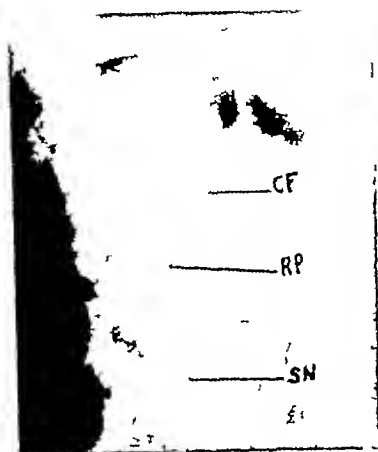


Fig 11

Fig 10 Photograph of a sagittally cut section of the spinal column from the same patient as shown in Figure 9. In the lumbar region the discs, *D*, are seen almost to touch.

Fig 11 A clinical roentgenogram showing a lateral view of the lower thoracic and upper lumbar regions of a patient who fell approximately 20 feet from a telegraph pole. Roentgenogram taken immediately after the accident was

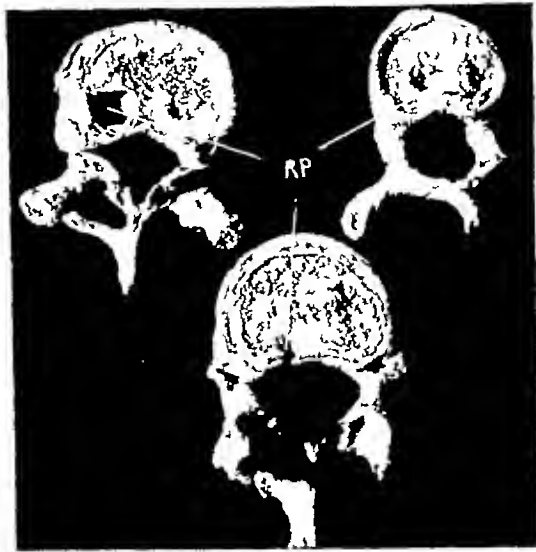


Fig 12

negative except for a compression fracture, *CF*, of the twelfth thoracic vertebral body, but this repeated view 3 months later revealed a rupture of the cartilaginous plate, *RP*, of the first lumbar body and a definite Schmorl's nodule, *SN*, in the second.

Fig 12 Photograph of three macerated vertebrae showing typical depressions, *RP*, produced by prolapse of nuclear tissue into the spongiosa.

### PATHOLOGY

1 *Thick discs* At birth, the discs are relatively thick as compared with the height of the vertebral bodies. However, as the spinal column elongates with the advance in age, the discs gradually become relatively thinner (Fig 8).

Also, in diseases which decrease the strength of the spongy bone, the pressure of the gelatinous nucleus in the intervertebral disc causes a bulging out into the adjoining vertebral bodies as is seen in such conditions as osteoporosis (Fig 9), osteomalacia, cancer metastasis, and myeloma. In such cases the spongiosa may be so soft that the intervertebral discs almost touch (Fig 10).

2 *Thin discs* Much more frequently than thick discs, one sees thin discs in roentgenograms of abnormal spinal columns. Sometimes the vertebrae appear almost to touch. It must be remembered that normally the intervertebral discs in the sacrum decrease during life until there is a complete disappearance except for the first sacral disc and sometimes the second which may persist to old

age. Occasionally a remnant of what might be considered a primitive disc separating the base from the body of the epistropheus remains until advanced age. With these exceptions, in any other part of the vertebral column, however, a change in height of the intervertebral space indicates a pathological change in the disc.

The decrease in water content of the disc which begins in the third and fourth decade, and all conditions which are collectively called degeneration, diminish the elasticity and make the disc thinner. Such transformations are usually accompanied by a color change in the disc substance, by cleft formation, and by fibrous tissue infiltration.

3 *Displacement of the intervertebral disc tissue* The prolapse into the bony portion of a vertebral body (Figs 11 and 12) which can be shown by roentgenogram is now commonly referred to as a "Schmorl's nodule." This condition was first described by Luschka.

Schmorl believes that the importance of these nodules has been overemphasized in

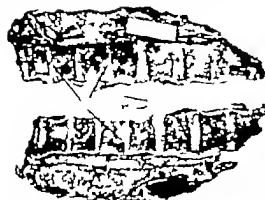


Fig. 3 Photograph of portion of two spinal columns placed side by side for comparison. The one below shows carcinoma metastases, the one above multiple myeloma. A disc in the one below has been sufficiently weakened to permit rupture of the nucleus pulposus, *N*, into the spongiosa of an adjoining vertebral body. In the column above, discs show slight narrowing with extrusion of some of their nuclear contents, *A*, into adjoining vertebral bodies.

medicolegal cases. Furthermore in this regard it is well to remember that it requires several months before a diagnosis of a ruptured nucleus pulposus can be ruled out. This is because a prolapse of disc tissue into the spongiosa is not demonstrable immediately afterward. In fact, the first change after such an injury is a fibrous tissue reaction. This is replaced after about a month by a rim of cartilage which later shows a deposit of calcium sufficient in amount to be seen in a

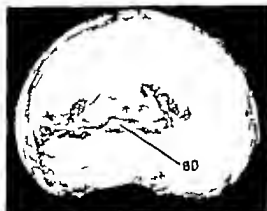


Fig. 5 Photograph of horizontally cut intervertebral disc, showing brown degeneration, *BD* from case 7 years old.



Fig. 14 A posterior view of section of the thoracic spine with the spinous processes removed showing small rupture of the nucleus pulposus, *N*, posteriorly into the vertebral canal. (N symptoms (from pressure on the spinal cord) are experienced by this patient.)

roentgenogram only after 3 to 4 months following the original injury.

Therefore final judgment regarding injury to a spine should not be rendered by a single X-ray examination when a displacement of disc tissue is a possibility.

The normal disc surfaces are thin where the nucleus pulposus bulges against them. It is here that less resistance permits rupture of disc substance into the spongiosa of the bodies. The causes of prolapse may be listed as follows: (1) The nucleus pulposus may follow old vessel channels which lead into the disc (Bohmig). (2) Degeneration may cause tears in the cartilaginous plates of old people. (3) Certain pathological processes may exist in the vertebral bodies in such conditions as tuberculosis, abscess formation, cancer metastases (Fig. 3), Paget's disease, osteoporosis, myeloma, penetrating notochord canal, or compression fracture which in young people may produce an irregular jagged tear in the cartilage plate.

These displacements of disc tissue not only decrease the height of the disc but lessen its elasticity, lower its efficiency and produce abnormal motion through release of pressure within the annulus—this may be compared to a partially deflated automobile tire. This may result in the grinding up of the remaining disc substance.

Posterior displacement of the nucleus pulposus may produce pressure on the spinal cord and lead to serious neurological disturb

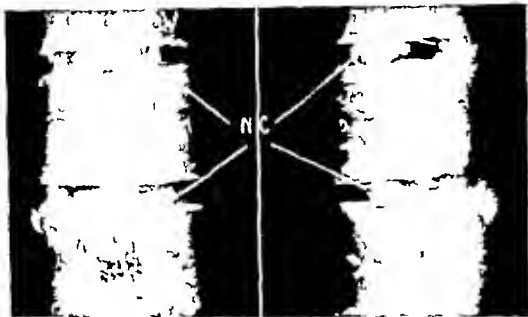


Fig 16 Anteroposterior and lateral roentgenograms of the eighth and ninth thoracic intervertebral discs from a woman of 52 years showing the nuclear clefts, NC, of the upper disc injected with mercury and the middle one with lipiodol, demonstrating marked dilatation of the disc spaces. The blood vessels are injected with mercury.

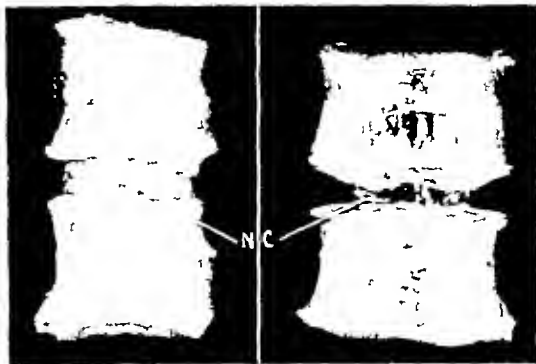


Fig 17 Lateral and anteroposterior roentgenograms of an injected intervertebral disc from a woman 89 years of age showing the laminated appearance of the nuclear clefts, NC.

ances resembling a cord tumor, as reported by Dandy, and Barr and Mixer, or may produce no clinical symptoms whatever (Fig 14) depending, of course upon the size and location of the protruding mass of disc tissue.

*4 Degeneration (driving out grinding up, and deposition of pigment)* Although the anatomical changes in the disc during degeneration vary greatly they cannot be detected clinically except when they are accompanied by a decrease in height or by a deposit of calcium, which conditions may be shown by roentgenograms. In a young person when the intervertebral disc is cut open, the gelatinous nucleus bulges out and appears moist, in an older person it appears dry and yellowish or dark brown in color (Fig 15). The composition of this pigment is not known, it does not give any reaction to the test for iron, for this reason it is believed to have no connection with blood. When the nucleus of an adult disc is injected with a substance opaque to roentgen rays, the resultant picture reveals a system of nuclear clefts, compared by one writer to the spaces between the lamellated layers of an onion, these are always much dilated in old people (Figs 16 and 17).

The grinding up of the intervertebral disc tissue produces large cavities in the interior (Fig 18), while the outermost periphery of the fibrous ring remains intact. Such resultant cavities are lined with a gray dry crumpled tissue which is the former disc substance dried up and ground up. Occasionally concentric

tears are found in the fibrous layers near the edge parallel to the rim ledge.

It is interesting in this regard to note that in hard working people, Schmorl reported well preserved discs even in the aged whereas in people who had sedentary occupations strangely enough, more often degenerative changes were found. He believed that ordinary trauma in daily work plus the individual constitutional factors which vary greatly in different individuals despite occupation or walk of life, play a more effective rôle than disease processes in producing these degenerative changes. At least this was the conclusion he was forced to take in trying to interpret his own statistical records.

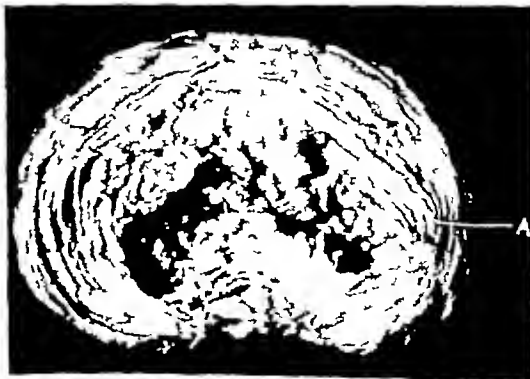


Fig 18 Photograph of a horizontally cut disc from a woman 85 years old. Only the outer layers of the fibrous ring, A, remain. The gelatinous nucleus and inner parts of the fibrous ring are ground up and destroyed.



Fig. 9. A clinical roentgenogram of the thoracic vertebral region in a patient who shows calcification. A, in one intervertebral disc; it should be noted here that practically every cartilaginous plate has been replaced.

**5 Calcifications.** Calcifications may appear in the soft regions of the gelatinous nucleus as cloudy spotty branched shadows usually in the central portion of the disc with several processes projecting outward, but they appear more frequently in the periphery of the fibrous ring. They can be demonstrated easily by roentgenogram (Fig. 19). From 200 carefully studied vertebral columns of all ages, Ratheke calculated that 71 per cent of these showing lime deposits were in the annulus and 6.5 per cent in the nucleus. The incidence of these



Fig. 20. Photograph of the anterior aspect of spine just as it appeared when removed at autopsy from a woman 52 years of age. A calcium deposit, A, D may be seen projecting between the teeth and clavish thoracic vertebrae. (A tied off portion of the aorta, B, bone was retained here for the purpose of injecting the arteries with mercury.)



Fig. 21. An anteroposterior roentgenogram of the same section of spine as in Fig. 20, showing bony spicules, K, in the aortic shadow. (The vessels, B, are shown injected with mercury.)

deposits increases with age. The etiology is generally regarded as a degeneration phenomenon except in the so-called "secondary calcifications" following healing inflammatory reactions (tuberculosis) but further research is necessary to show whether they are merely calcified hematomas.

**6 Deposits in the intervertebral discs of other kinds of tissues.** Fibrous tissue has been reported found in the gelatinous nucleus post-mortem at autopsy. Such deposits destroy the normal stratification of the nucleus and possess very little elasticity. Clinically one finds a decrease in the height of the disc.

Blood vessels occasionally occupy a considerable part of the gelatinous nucleus and fibrous ring. Connective tissue generally accompanies these vessels which arise usually from the surfaces of the vertebral bodies. The borderline between the disc and the ingrowing blood vessels is quite distinct. This invading tissue may not always be in the gelatinous nucleus but may be in the annulus. Here it represents a process of healing concentric tears in the outer portions of the fibrous ring.

The ingrowth of blood vessels and fibrous tissue is often accompanied by bone formation. The intervertebral disc may be completely replaced by spongy bone as in the congenital "block vertebra." Sometimes a little remnant of the disc tissue may be present.

Occasionally the region of the annulus may be filled with spongiosa while the mid-portion of the disc still contains the gelatinous nucleus. Because they are sometimes confused with fractures of the rim ledge, it is important from the standpoint of differential diagnosis to distinguish between these deposits of calcium in the annulus following little tears in the fibrous ring. Such deposits occur most frequently on the anterior border, parallel to the stratification of the fibrous ring, and may be quite large (Figs 20 and 21)

The author is indebted to Dr Frank R Ober for his helpful suggestions in directing this work, to Dr Sidney Farber for the use of his laboratory, and to Dr G Kenneth Coonse for permission to use two of his clinical X ray pictures

## BIBLIOGRAPHY

- 1 BARR, J S, and MILNER, W J Rupture of the intervertebral disc with involvement of the spinal canal *New England J Med.*, 1934, 211 210
- 2 BEADLE, O A The Intervertebral Discs Observations on their Normal and Morbid Anatomy in Relation to Certain Spinal Deformities *Medical Research Council, Special Report Series, No 161, London, 1931*
- 3 DANDY, W E Loose cartilage from intervertebral disc simulating spinal cord tumor *Arch Surg*, 1929, 19 660
- 4 KEYES, D C, and COMPERE, E L Normal and pathological physiology of nucleus pulposus of intervertebral disc. *J Bone & Joint Surg*, 1932, 14 No 4
- 5 RATHEKE, L, Ueber Kalkablagerungen in den Zwischenwirbelscheiben *Fortschr d Roentgenstr*, 1932, vol 45
- 6 SCHNORL, G and JUNGHANS, H Die Gesunde und Kranke Wirbelsaenle in Roentgenbild *Leipzig Georg Thieme, 1932*

## GASTROJEJUNAL ULCER AND GASTROJEJUNOCOLIC FISTULA

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IN 1928 one of us (FHL) and Dr Sara M Jordan published a survey of the literature on gastrojejunal ulcer and reported cases from this clinic<sup>1</sup> About one thousand cases had then been reported but gastrojejunal ulcer was not accepted at that time by many surgeons as a common complication of anastomosis of the jejunum to the stomach In the years 1928 to July, 1934, there have been 1,089 cases of gastrojejunal ulcer reported in the literature

It is interesting to note that gastrojejunal ulcer is now considered a serious and not unlikely complication of any operative procedure for ulcer in which the stomach is anastomosed to the intestine, and not a sequela peculiar only to gastro-enterostomy

## INCIDENCE

As can be seen in Table II the reported incidence of gastrojejunal ulcer varies greatly The range for gastrojejunal ulcer following gastro-enterostomy is from 17 per cent (Walton) to 24 per cent (Strauss, Block,

Friedman) With resections there is also a wide disparity in its incidence from 0.4 per cent (Schwarz) to 10 per cent (Gatewood) It is noteworthy that the German investigators report a very low incidence of marginal ulcer following resection Fohl ascribes these variations in incidence to incomplete follow-up studies and possibly to the number of ill-advised operations rather than to constitutional characteristics or operative technique

Hurst and Stewart believe that the incidence of gastrojejunal ulcer is greater than is reported, and base their opinion on results of a statistical study of postmortem examinations at the New Lodge Clinic In a series of 10,300 autopsies, there were 131 on patients who had had operations for ulcer Of these, 46 patients died within 10 days of the operation for ulcer and in these patients there were no gastrojejunal ulcers In 41 cases death occurred from 10 days to 2 months after operation In this group there were 3 gastrojejunal ulcers In 43 cases in which death occurred 9 months after operation, there were 22 cases of ulcer All of these gastrojejunal

<sup>1</sup>Lahey Frank H. and Jordan Sara M. Gastrojejunal ulcers and gastrojejunocolic fistulae. *Ann Surg* 1928 Feb

TABLE 1

Name	1928	Cross	Total	Name	Cross	Total
Allen				Yeller	3	
Balfour				Oberniedermayr	4	
Broster	6			Starbinger	7	
Bucke	6			St. John		
Deaver				Walton	44	394
Elrich						
Grassbach					931	
Harrist, Stewart	44			Allen		
Jones	36			Chandler		
Lepiat				Da. export		
Laura				Dona	3	
Nixon, Lowry				Flasterer		
Parsack				Hinton	7	
Reiterman				Jadis		
Robinson				Lewicki		
Schwartz				Lubin		
Strauss, Wack,				Romell		
Friedman	5			Sorytk		
Stefinger				Steden	4	
Thompson,				Viviana	5	
Stewart		3		Walsh		
				Woodside	1	
	929			Zakowewitz,		
				Eck		78
Bayer	3					
Balfour	3				93	
Cabot Case				Bertand, Marten		
Emerson, Smith	4			Braun		
Froehne				Bruckner		
Gottlieb				Tobias		
Hayes				Buckstein	3	
Huttenlocher				Canica		
Jadis				Connell		
Jest				Ester		
Lenche				Marqure		
Loff	48			Prickman		
Emson				Valdieu	5	66
Sole	3					
Urrutia	29				933	
Weir	13	390		Andrews		
				Balfour		
	930			Benedict	30	
Balfour	16			Darton	3	
Bromley				Larson		
Douglas				Mallet, Gay		
Emmely	3			Meyer, Rom		
Emmy Hanna				Miller, Hobsone		
Linn	20			Strada		
Gatwood	9			Wills		43
Haberer						
Hartwell, Felter					934	
Horsley	3			Steinberg		
Jachne	4			Wallace		
Lewicki	5			Walton	19	84
Total number of Cases						1,089
BUDGET						
928	3	93				66
929	390	933				48
930	203	934				8
93	78					
		Total				660

figures the total incidence of gastrojejunal ulcer in 131 ulcer operations to 10 per cent.

Because of the high incidence of gastro-jejunal ulcer after operations in which the pylorus is separated and occluded (20 per cent Blackham, Leriche v Haberer) operations of that type (such as von Eiselsberg's exclusion) have largely been abandoned. It is difficult to compare the incidence of recurrence of ulcer after anterior and posterior gastro-enterostomy although most authors state that recurrence is more frequent after anterior anastomoses. However Walton in 1313 posterior anastomoses found 29 gastro-jejunal ulcers while in following 33 patients with anterior gastro-enterostomies there were no marginal ulcers. Fischer believes that postoperative ulcer does not occur more often following anterior gastro-enterostomy and urges its use to avoid the complication of fistula into the colon (Gastric jejuno-colic fistula). Allen believes that marginal ulcer occurs as frequently after resection as after gastro-enterostomy and in addition a secondary operation is more difficult after a resection.

In a paper by Dr Roscoe R. Graham, of Toronto, Canada, read at the last meeting of the American Medical Association and kindly made available for us by Dr Graham before its publication, the results of a series of gastric operations as relates to gastroduodenal and jejunal ulcer are presented. These results are based upon 43 cases of which 33 were personally operated on by Dr Graham. This included 4 cases of gastroduodenal fistulas. Of the 43 cases, 4 cases, they state, had been studied and confirmed by X-ray examination, but not yet operated upon. Six were cases of associates. Five of these 6 cases were proved by operation and one confirmed by X-ray.

In a series of 5 cases in which the stomach was cut across at its middle, the distal end turned in and the jejunum anastomosed to the proximal end, the so called Devine procedure, he surprisingly reports the development of 3 jejunal ulcers in a relatively short time.

Three cases are reported in which the gastroenterostomy was taken down with excision of the ulcer repairing the defect in the duodenum.

thus restoring the alimentary canal to its original state. All 3 cases, he states, are now suffering severely from duodenal ulcer symptoms.

Of 28 cases with primary pyloroplasty for duodenal ulcer, the author states that in subsequent X-ray studies in none did they find normal gastric motility. They report constant hyperperistalsis and state that the patients have not had brilliant clinical cures.

In 9 cases in which the stomach was anastomosed to the duodenum (gastro-duodenostomy) there was one fatality and 4 instances of marginal ulceration at the stoma.

In 4 cases in which the gastro-enterostomy was taken down, the jejunum restored, a partial gastrectomy done, and the end of the stomach anastomosed to the second part of the duodenum, there were 3 instances of ulceration at the new stoma.

In 1 case a partial gastrectomy was done with restoration of the jejunum, an anterior Polya anastomosis and an entero-enterostomy with the development of an ulcer in the efferent loop of the Polya gastrojejunostomy.

They report no recurrences after gastric resection, restoration of the jejunum, and end-to-end anastomosis of the cut end of the stomach to the duodenum and no recurrences following resection and posterior Polya anastomoses.

The figures of Hinton and Church published 1 month ago are of great interest because of the fact that all of the cases have been so well worked up and so carefully followed. The report is from the Fourth Medical and Surgical Division of Bellevue Hospital. Ninety patients of all the admissions for ulcer from January 1, 1928, to January 1, 1933 had been operated upon. Of these 79 had had gastro-enterostomy. Of these 79 patients having had gastro-enterostomy, 13, or 16.4 per cent, had gastrojejunal ulcer. Of these patients considered to have gastrojejunal ulcer, 6 were proved by operation to have it and 7 by X-ray evidence to have it, and it must be admitted from the convincing X-ray evidence which is recorded in each case that it seems likely that the diagnosis was correct also in these cases.

Walton states "There seems no doubt that a partial gastrectomy does not give a com-

TABLE II—INCIDENCE OF GASTROJEJUNAL ULCER

Year	Name	Gastro enterostomy			Resection		
		No of gastro-enterostomies	No of anastomatic ulcers	Per cent	No of operations	No of anastomatic ulcers	Per cent
1929	Rowlands			2			
	Schwarz			3-5	210 (Reichel)	1	0.4
	Strauss						
	Block			24	Polya		1
	Friedman						
1930	Balfour	491		3.20			
	Luff	744	21	2.8			
	Weir				418	33	7.8
1931	Berg						11
	Halberer				2310	15	0.6
	St John	119		6.9	76		3.6
	Walton	951	44	4.7			
	Neller				43	3	7
	Starlinger				2564	113	0.7
	Gatewood	146	9	6	30	3	10
	Charrier	60	2	3.3			
1932	Pauchet			5			
	Fischer						15-† 5.6
1933	Benedict	73		2.9			
1934	Wilkie			3.5			
	Walton	1576	30	1.60	326	2	61
	Hinton	79	13	16.4			

From 85 institutions  
†From literature.

plete immunity to the onset of the gastrojejunal ulcer, but it is less frequent after this operation (about 0.5 per cent) than after gastro-enterostomy." He states "My own belief is that, provided sufficient of the stomach is removed to produce achlorhydria, the complication is almost unknown, although the risk of subsequent anemia may be increased thereby."

Our own experience with gastrojejunal ulcer and gastrojejunal colic fistula deals with 30 gastrojejunal ulcers and gastrojejunocolic fistulas of which 13 were uncomplicated gastrojejunal ulcers and were operated upon. The immediate mortality in this group was 2 cases, 15 per cent. Of the 13 patients operated upon, 10 had excision of the gastro-enteros-



tomy resection of the jejunum anastomosis of the jejunum, and restoration of the alimentary stream to its normal state. Of the 10 patients having this operation 40 per cent or 4 have had recurrent duodenal ulcers. Of these 4, 1 died later of an acute perforation, 1 had severe symptoms of duodenal ulcer 11 years afterward, but had not been able to follow a careful regimen, 1 was well for 4 years and then had a serious hemorrhage, and on 1 a radical subtotal gastrectomy was done (FHL) 2 years after the conservative operation.

Of this group there are 9 patients with gastrojejuno-colic fistula 1 of whom refuses operation and 8 have been operated upon. The immediate mortality was 63 per cent, the cause of death being in 1 case peritonitis in 2 pneumonia 1 was a cardiac failure, and 1 was due to obstruction and pneumonia. Of the living cases of gastrojejuno-colic fistulas, 1 patient is perfectly well 5 years after operation but on a strict diet 1 is well at the end of 2 years, 1 died of obstruction 4 months after leaving the hospital, and the 1 who refused operation has been followed 8 months, and is having one to two stools a day and is in excellent health.

There are 8 cases proved by X ray diagnoses and histories of gastrojejunal ulcer in which operation was not done of these 3 are well 6 8 12 months, respectively after first being seen and placed on treatment. One has now gone 4 years but has severe ulcer symptoms which can in a considerable measure be controlled by treatment, 1 has been under observation but 6 months and is unable to work 1 died from an acute perforation 2 years after being on treatment, 2 are well but have had serious hemorrhages 1 at 2 years and 1 at 4 years after the onset of symptoms. It must be admitted I think that there are some patients with gastrojejunal ulcer and also a few with gastrojejuno-colic fistulas who can be carried along satisfactorily under medical measures.

#### AGE

The age incidence depends upon the age at which the primary operation was done, but in a large majority of the cases listed the patients are in the age period from 30 to 45

years. The youngest in this survey was in a boy of 10 years, reported by Strode. From three fourths to four fifths of all cases reported are in men. (Hayon) In our series there were 90 per cent males and 10 per cent females.

#### PATHOLOGY

The postoperative (gastrojejunal) ulcer occurs for the most part at one of two sites—either at the stoma itself or in the efferent loop of the jejunum in the neighborhood of the anastomosis, often opposite the new opening. They are all in the jejunum either marginal to the new opening or at a little distance from it. Gastrojejunal (marginal) ulcer is found in 75 per cent of the cases, and jejunal in 25 per cent (Urrutia, Starlinger).

They are similar pathologically to primary peptic ulcers, in that they are sharply demarcated and are very vascular. Ulcers of small size show a very intensive proliferative reaction about them which results in a definite tendency to penetration into neighboring organs. The earlier authors reported the incidence of perforation in gastrojejunal ulcers as 30 to 35 per cent. However Gottstein, Just Gosset, Bertrand Martin all believe that it is comparatively rare. Starlinger reported the number of collected cases of free perforation as 150. On the basis of 1,500 cases of gastrojejunal ulcer reported after gastro-enterostomy and 300 after resection, he estimated the percentage of perforations as 5.6 per cent after gastro-enterostomy and 3.3 per cent after resection. The percentage of perforation in our series was 9 per cent.

Makkas (1934) collected 170 cases of free perforation from the literature. He believes that perforation occurs less frequently in gastrojejunal than in primary peptic ulcer probably because the severity of the symptoms leads patients with gastrojejunal ulcer to seek help from surgical treatment earlier than do those with duodenal and gastric ulcer. This complication occurs most often in jejunal ulcers (Bager Makkas). Gastrojejunal ulcers show a considerable tendency to hemorrhage, in our series 3 per cent.

#### ETIOLOGY

Numerous theories have been proposed to explain the occurrence of gastrojejunal ulcer

Among these are ulcer diathesis, hyperacidity, infections, poor surgical technique and the lack of medical care

One of the most fundamental of these theories is that of ulcer diathesis, a constitutional tendency on the part of an individual to develop ulcer. This tendency is particularly evident in this group of patients with gastrojejunal ulcers in many of whom a series of operations had been done for recurrent ulcer. A brief history of one of our own cases illustrates this point

Mr R. A. A gastro-enterostomy was done on this patient by one of us (FHL) for duodenal ulcer in 1917 with the development of a gastrojejunal ulcer which was operated on by FHL in January, 1928. The ulcer, gastro-enterostomy opening, and a section of the jejunum were removed, and the alimentary canal restored to the original course with the immediate development of an active duodenal ulcer with bleeding that required further operative procedure. In May, 1929 the stomach was cut across at its center, a large section of stomach removed, the jejunum anastomosed end-to-side to the proximal cut end of the stomach and the distal cut end turned in (Devine operation). No attempt was made to remove the ulcer because of the immense amount of induration about it. Following this operation, there have still been ulcer symptoms associated with gastric hemorrhages. This patient seen 2 days ago, 5 years after operation, has gained 18 pounds in weight but requires strict adherence to a limited diet to remain free from ulcer symptoms.

High family incidence is another indication of this tendency. Allen reported a family in which the father and 5 sons all had an ulcer history, with numerous operations. Hurst and Stewart found that in 6 of 43 cases there were 2 or more near relatives who had gastrojejunal ulcer. Jones also found a striking family incidence of ulcer in a group of cases of gastrojejunal ulcer.

A significant contribution to the possible etiology of gastrojejunal ulcer has been the explanation according to the biochemical theory of the nature and location of ulcer lesions.

Buenger has pointed out that areas in the stomach which secrete acid gastric juices are somewhat resistant to ulcer formation, while areas of gastric activity protected only by the mildly alkaline mucous production are highly susceptible to ulcer formation.

After operative procedures such as gastro-enterostomy where the jejunum is brought into contact with an area of gastric activity near the pyloric end of the stomach, a severe jejunitis occurs according to Konjetzny and Puhl. This is shown by increased connective tissue in the submucosa, definite dilatation of vessels, and the infiltration of surrounding tissues with inflammatory cells.

However, Walters believes that the type of ulcer seen in Germany is different from that commonly seen in this country, being characterized by multiplicity of ulcers and extensive erosions. These changes regarded as characteristic by German authors, he has found in very few patients in this country. He raises the question as to whether the small percentage of recurrences after gastro-enterostomy reported by some authors in this country may not be in cases in which such a gastritis has occurred.

At von Bergmann's clinic changes in the mucous membrane of the jejunum have been noted in all cases of gastrojejunal ulcer.

One might suppose that some light on the causation of postoperative ulcer might arise from a study of primary jejunal ulcer but such is not the case. While this lesion is unusual Ebeling in 1933 reported 47 cases collected from the literature. This condition occurred in the 40 to 60 year group, with a preponderance of 3 to 1 in males. The history was of dyspepsia, often simulating a duodenal or gastric ulcer history. The ulcers were located in the upper or middle jejunum and were similar pathologically to gastric or duodenal ulcer. Any specific cause was eliminated in the cases reported as far as possible. That an excess of acid secretion may be a factor is suggested by the case of Holzweissig mentioned by Morrin, in which 8 ulcers occurred in the jejunum in the presence of a complete obstruction by a stone at the ampulla of Vater.

#### HYPERACIDITY

Unquestionably, hyperacidity plays a prominent rôle in the etiology of gastrojejunal ulcer. There are numerous clinical and experimental observations which indicate the importance of this factor.



Fig. The X-ray picture which was reversed in printing demonstrates very clearly the barium filled crater of post-gastroenterostomy jejunal ulcer. The ulcer may be seen as diverticulum like projection from the jejunum just beyond the point where the jejunum has been anastomosed to the stomach bearing out the statement in the text that these ulcers are all jejunal, 75 per cent being marginal to the gastro-enterostomy and 25 per cent in the jejunum at varying distances from the stoma.

1. Gastrojejunal ulcer occurs but rarely in women. Lerman, Pierce, and Brogan after histamine and alcohol tests found that in a normal group males show a higher acidity range than females.

2. Gastrojejunal and postoperative jejunal ulcer almost never occurs after gastro-enterostomy for carcinoma, a condition in which anacidity is usually present.

3. The primary ulcer in a large proportion of cases is duodenal. In our series the primary ulcer was duodenal in 90 per cent of the cases and gastric in 10 per cent. Hurst and Stewart found that 61 per cent of duodenal ulcers were accompanied by hyperacidity while only 20 per cent of gastric ulcer showed increased acidity.

4. Gosset found that 80 per cent of his cases of gastrojejunal ulcers had hyperchlorhydria. Jones found that 74 per cent were above the normal level. In our series

95 per cent of our cases had a hyperchlorhydria. In those patients in our series with a gastrojejuno-colic fistula but 50 per cent had a hyperchlorhydria.

5. Rivers and Wilbur reported 7 cases in which gastro-ileostomy had been done by mistake before the patients came into their hands. In 2 of these ulceration was present in the ileum. Their conclusion was that peptic lesions may arise in any situation in which gastric juices are allowed to come into contact with intestinal mucosa.

6. Indirect evidence is afforded by a case reported by Morton and Graham. A patient had been operated upon for cholelithiasis. After operation she had a large hemorrhage and died. At postmortem examination a large duodenal ulcer was found and two stones blocking the bile duct and the pancreatic duct so that no alkaline digestive juices were reaching the pylorus.

7. Owings and Smith repeated the experiments of Mann and Williamson and reported that 10 of the 26 dogs developed ulcers of the jejunum when the jejunum was deprived of the alkaline digestive juices. Their work indicated that bile was the most important element in the neutralization of acid chyme.

8. That the influence of acid secretions is not the sole factor is suggested by the case which Eusterman reported in which gastrojejunal ulcer developed in the presence of persistent achlorhydria.

#### INFECTION

The influence of foci of infection on the causation of ulcer is generally accepted if not proved.

Hurst feels that infection is the most important exciting cause of gastrojejunal ulcer. The focus may be in the teeth, pharynx, sinuses, appendix, or gall bladder or in a gastric or duodenal ulcer which has not healed. In his series of 36 cases, he found only 2 with normal teeth.

Wilkie believes that ulcer can be considered one of many septic foci and no treatment is of lasting benefit until these foci are removed. He stresses particularly dental infection.

Saunders reports the recovery of a streptococcus from 16 cases of resected gastroduo-

denal and gastrojejunal ulcers, which was identical and specific by differential cultural and agglutination tests. The growth of the organism was inhibited by bile.

#### POOR SURGICAL TECHNIQUE

The most frequently mentioned possible causative factors in surgical technique in the production of postoperative gastrojejunal ulcer are the use of non-absorbable sutures, the use of clamps, and the improper placement of the anastomosis.

Scott, by clinical and experimental records, showed that sutures did not influence the occurrence of ulcer. In our earlier paper on this subject (Lahey and Jordan), it was likewise our conclusion that suture material played no part in the production of ulcer. The frequency of postoperative ulcer has increased in recent years despite the general abandonment of non-absorbable sutures. Several cases are reported in which strands of suture were found hanging from the anastomosed mucosa in the complete absence of any ulcer. Any ulceration at the stoma will of necessity erode down to the suture line and if it is of linen or silk this will be visible in the ulcer base.

Andrews does not believe that sutures have any influence. Walton states that the use of catgut may reduce the incidence, but it will not abolish it.

Willis states that "from later observations it is likely that silk or linen suture is simply a bystander and not the cause of the lesion."

Tight clamps are seldom used in operations on the stomach at the present time, so that their influence on the formation of ulcers is probably negligible.

In regard to operative trauma, Balfour is convinced that some recurrences are due to the devitalization of the suture line. This, however, does not explain the occurrence of gastrojejunal ulcer 10 to 15 years after the gastroenterostomy.

The position of the anastomosis high on the gastric wall theoretically leads to stagnation of the stomach contents and poor emptying. Hartwell and I later do not think the location of the gastroenterostomy opening has either an important clinical or mechanical influence



Fig. 2. The X-ray print needs very little explanation. This is a bismuth enema in a patient with a large gastrojejunal fistula in which all of the structures can be readily recognized. Note the size of the fistula into the colon. Note the large amount of bismuth in the stomach and its fluid level. From this amount of bismuth it must be concluded that the caliber of the fistula must be considerable.

as they found patients in their follow up study by X-ray examination who had high openings but no complaints and satisfactory emptying time. Benedict reported a case in which recurrence of ulcer followed 18 years of freedom from symptoms in which the stoma was located high on the gastric wall. We have had a patient in whom gastrojejunal ulcer occurred 17 years after a gastro-enterostomy.

These opinions together with some of our experiences and excerpts from a further review of the literature (1928-1934) are recorded in order that readers may have some idea of the conflicting opinions and variety of theories available in connection with this subject.

#### SYMPTOMS

The time of onset of symptoms of gastrojejunal ulcers varies from a few weeks to many years up to 21 years (Lublin). In 50 cases

taken at random, 50 per cent of the recurrences (gastrojejunal) occurred within 2 years following operation.

In general it may be said that the longer period patients who have had anastomoses of the jejunum to the stomach go without recurrence of ulcer symptoms, the less likelihood is there of the occurrence of gastrojejunal or jejunal ulcer. One must assume, in spite of this, however, that in any patient who has had the jejunum anastomosed to the stomach, the development of a gastrojejunal ulcer is always possible regardless of the time factor.

There are certain features of the symptomatology of gastrojejunal ulcer which are characteristic of this condition. In patients who have developed postoperative gastrojejunal ulcer there is usually a period after the performance of the gastro-enterostomy in which the patient is entirely relieved of the ulcer symptoms for which the operation was done, with a later return of ulcer symptoms not infrequently of greater intensity than the original symptoms for which the operation was done. The ulcer pain is less satisfactorily relieved by food and alkalines than was the pain associated with the original ulcer. The pain is less consistently related to meals than was the original ulcer pain. The distress associated with the occurrence of gastrojejunal ulcer is less tractable to all methods of treatment than was the distress associated with the original ulcer.

Hemorrhage and melena are, we believe, somewhat more frequently associated with marginal ulcer than with the duodenal and gastric ulcer.

The point of abdominal tenderness in duodenal ulcer (and duodenal ulcers make up the great majority of ulcers, so duodenal to 1 gastric ulcer in our experience) is usually in the right upper quadrant while in gastrojejunal ulcer the point of abdominal tenderness tends to be lower down a little above and to the left of the umbilicus. This is the point on the abdominal wall opposite which the anastomosis of the jejunum to the stomach commonly rests and with gastrojejunal ulcer it is usually tender over the stoma here.

Symptoms of ulcer perforation in any patient who has had a gastro-enterostomy per-

formed particularly for duodenal ulcer should make one suspect the possible presence of a perforated gastrojejunal ulcer.

#### DIAGNOSIS

The recurrence of symptoms suggestive of ulcer after operative measures for ulcer particularly duodenal ulcer should always suggest the probability of gastrojejunal ulcer. The presence of tenderness over the stoma on fluoroscopic visualization of the stoma likewise suggests it. The presence of a fecal at the stoma after the ingestion of a small amount of barium suggests that this is due to a small amount of bismuth remaining adherent to the ulcer (Fig. 1). The presence of a gastrojejunal fistula demonstrable by X-ray definitely settles the diagnosis of gastrojejunal ulcer (Fig. 2).

The closure of the stoma likewise suggests the presence of a gastrojejunal ulcer as does persistent deformity of the stomach, stoma or jejunum.

#### PROPHYLAXIS

There is probably no really effective prophylaxis against the possible occurrence of gastrojejunal ulceration following anastomosis of the jejunum to the stomach. Exclusive of the immediate technical steps of the operation of anastomosis of the jejunum to the stomach such as tight sutures, tight clamps, and non-absorbable sutures all of which can as already stated probably be excluded there are a number of things which at least are factors favorable to the postoperative occurrence of a gastrojejunal ulcer.

We have repeatedly stated that any patient who has an anastomosis of his jejunum to the stomach should be told of the danger of post-operative marginal ulcer. He should be told of the seriousness and intractableness of such a complication and the need for permanent modification of eating, drinking, smoking and living habits after any gastric operation for peptic ulcer. There has very definitely been an improper tendency to let patients assume that one of the rewards of a successful operation for peptic ulcer is that they escape the necessity of the above mentioned life-long modification of life habits. Unless such a warning is given patients, should a recurrent

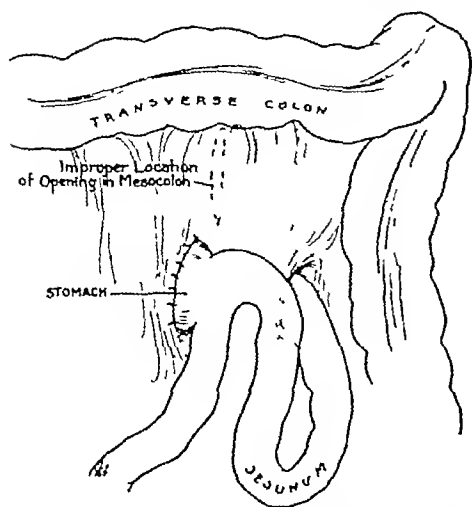


Fig 3 This illustration shows diagrammatically the proper and improper location of the opening in the gastrocolic omentum for a gastro-enterostomy. One can appreciate when the opening is made as shown in dotted lines close to the transverse colon, that should a gastrojejunal ulcer occur, it almost must involve the transverse colon in the surrounding exudate and so penetrate frequently into the colon and produce a gastrojejunal fistula. This drawing illustrates a jejunal loop of sufficient length to permit easy resection and anastomosis should a jejunal ulcer occur as opposed to the no-loop type of jejunal anastomosis.

gastrojejunal ulcer occur, no surgeon's conscience can be entirely free from responsibility for this recurrence. While no statistical figures are available as to the incidence of gastrojejunal ulcer following gastro-enterostomy in patients with well controlled post-operative habits and diets as opposed to those with uncontrolled habits and diets, it is not unreasonable to assume as distinctly probable that the incidence of gastrojejunal ulcer will be less in those patients with gastro-enterostomies whose habits and diets are controlled than in those whose habits and diets are not controlled. This we have always maintained is perhaps a small but important factor in the postoperative incidence of gastrojejunal ulcer.

There are a few general surgical principles which probably influence the occurrence of gastrojejunal ulcer.

It is generally accepted that gastrojejunal ulcer is more apt to follow the employment of gastro-enterostomy in young individuals with high gastric acids and active ulcer symptoms

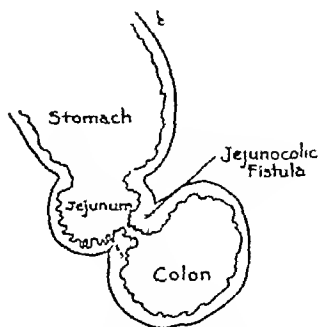


Fig 4 This drawing indicates diagrammatically how the colon becomes adherent to the jejunum and the ulceration breaks into it.

than in older people without strikingly high acids.

It is generally felt (as stated from the literature in this and our original paper) that to make a gastro-enterostomy and then to obstruct the pylorus preventing thus the regurgitation of alkaline duodenal contents into the stomach increases definitely the risk of gastrojejunal ulcer.

It is believed and is probable that to do entero-enterostomy between the afferent and efferent loop of a jejunum anastomosed to the stomach, sidetracking as it does the passage of alkaline jejunal contents from going back into the stomach through the new opening, likewise predisposes to an increased danger of the formation of a gastrojejunal ulcer.

It has been quite definitely demonstrated by animal experiments that the lower the level in the jejunum at which that structure is anastomosed to the stomach, the easier it is to produce intestinal ulceration since adaptability to receive unneutralized acid gastric contents is less and less well developed the further away that level is from the duodenum. For this reason, while no convincing figures are available to prove it, it is believed that anterior gastro-enterostomy requiring as it does anastomosis of the jejunum at a much lower level in the jejunum than is necessary with posterior gastro-enterostomy is perhaps followed by a few more gastrojejunal ulcers than is posterior gastro-enterostomy (Walton's figures of 33 cases with no gastrojejunal ulcers are suggestive but too small a series to be of great value). On purely theoretical grounds

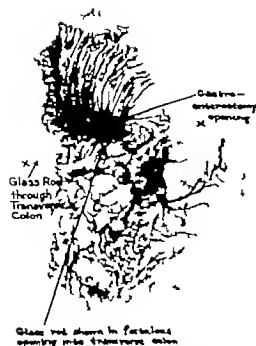


Fig. 5. This is the resected stomach of the patient whose X ray film is shown in Figure 4. The stomach is shown with the gastro-jejunocolic protruding. A glass rod has been passed through the attached transverse colon, *x-x*, and in the gastro-jejunocolic stoma the rod may be seen at the point where the jejunal ulcer has eroded into the colon. Although the photograph does not demonstrate it, all, one can from this picture of the block of tissue removed, stomach, colon and jejunum, get some idea of the amount of induration present.

If it could be proved that gastrojejunocolic ulcer was no more common following this operation than posterior gastro-jejunocolic would be a safer operation than posterior gastro-jejunocolic since, because of the position of the colon, gastrojejunocolic fistula with its high mortality is anatomically less apt to occur after anterior gastro-jejunocolic than after posterior gastro-jejunocolic and should gastrojejunocolic ulcer occur after anterior gastro-jejunocolic it would be infinitely easier and safer to manage surgically from a technical point of view than is gastrojejunocolic ulcer in posterior gastro-jejunocolic. Should a gastrojejunocolic ulcer occur with an anterior gastro-jejunocolic it occurs on the anterior wall of the stomach where it is easily approached and

In addition there is a long loop of jejunum available permitting the ready excision of the segment anastomosed to the stomach and with sufficient length of proximal jejunal stump so that end-to-end anastomosis can easily be done.

One of the greatest technical difficulties is dealing with gastrojejunocolic ulcer in posterior gastro-jejunocolic particularly if of the so-called no loop type, is that the induration about the ulcer involves the root of the jejunal mesentery at the level of the ligament of Treitz making separation of the jejunum and the handling of its mesentery with its blood supply difficult and the other is that when the jejunum is separated from the stomach if complete resection of a segment of jejunum is necessary such a small intraperitoneal proximal stump of jejunum sometimes remains that end-to-end anastomosis is often difficult and far from satisfactory.

It is definitely the opinion of one of us (FHL) that were he to select the type of gastrojejunocolic ulcer he preferred to deal with from his operative experiences with gastrojejunocolic ulcer he would select a gastrojejunocolic ulcer in an anterior gastro-jejunocolic and, if he had to have a gastro-jejunocolic he would feel safer with an anterior than a posterior one.

The complications of perforation and hemorrhage in gastrojejunocolic ulcer have already been mentioned but there remains to discuss the most serious, the most distressing, and from the point of view of management, the most perplexing of all the complications associated with this condition, that is, the perforation of the anastomotic marginal ulcer into the transverse colon producing a gastrojejunocolic fistula.

The mechanism of the production of a gastrojejunocolic fistula is first the occurrence of a gastrojejunocolic ulcer at a gastro-jejunocolic stoma. With these ulcers there is usually associated a large area of inflammatory induration extending well out from the ulcer area into the root of the mesentery.

Gastrojejunocolic fistula occurs almost solely in posterior gastro-jejunocolic. The posterior anastomosis of the jejunum to the stomach is often unwisely made through a

low opening in the posterior leaf of the gastrocolic omentum close to the transverse colon. This then results in the anastomosis resting close to, or in contact with, the transverse colon (a frequent technical error). The opening in the transverse mesocolon should be high (Fig 3), thus keeping the anastomosed jejunum away from the transverse colon. The exudate from the gastrojejunal ulcer soon extends to the transverse colon, includes that structure in the inflammatory mass about the ulcer, and soon perforates into that structure. This complication is said to occur in about 11 per cent of the cases.

Gastrojejunocolic fistulas probably cannot occur except in patients who have had a gastrojejunal ulcer for some time. The condition is to be suspected in any patient who has had a gastro-enterostomy particularly for duodenal ulcer followed by a return of ulcer symptoms and with belching of gas with a fecal odor, with persisting diarrhea due to the dumping of undigested food through a large fistulous tract from the stomach into the transverse colon. This condition is to be suspected in such a patient also who in spite of a good food intake is progressively losing weight, likewise, due to the direct passage of food into the transverse colon from the stomach and so failure to be utilized.

We have seen gastrojejunocolic fistulas varying in size from that of a pencil point up to the size of a silver dollar, so that bismuth given by mouth passed rapidly into the colon and a bismuth enema passed quickly from the colon to fill the stomach. In proctoscopy a patient suspected of having a gastrojejunocolic fistula who had had tapioca for lunch, we have found tapioca in the rectum at four o'clock of the same afternoon.

The diagnosis of large gastrojejunocolic fistulas by X-ray as shown in Figure 2, is easily made. In small fistulas, however, the X-ray diagnosis can be made with considerably less certainty. The mechanism of the perforation of a jejunal ulcer into the colon is diagrammatically shown in Figure 4.

#### TREATMENT

There is a distinct conviction on the part of most persons dealing with ulcer that pa-

tients with gastrojejunal ulcers seldom respond satisfactorily and permanently to medical treatment, but in all cases medical treatment should be carried out to reduce acidity thus perhaps lessening the area of acute reaction about the ulcer and improving the general condition of the patient as an operative risk. In addition, we have a number of patients with undoubted gastrojejunal ulcer who have been able to get along satisfactorily for a number of years on medical treatment.

Since any patient who has developed a gastrojejunal ulcer has demonstrated that he falls in the group of patients who are particularly liable to recurrent ulcer, it is the feeling of many surgeons and it is our conviction that any surgical measure short of radical subtotal gastrectomy will be likely to be followed by a recurrent ulcer and, as shown in figures from the literature, even with radical partial gastrectomy recurrent gastrojejunal ulcer will still occur in a small percentage of cases. In defense of this position one must admit that the best operative procedure for such recurrent ulcers is the one which is followed by the most complete post-operative anacidity and that operation is undoubtedly subtotal gastrectomy. The mortality, however, in such an extensive operation as is necessary with gastrojejunal ulcers and on patients frequently in poor condition, is considerable, reported by one of its ardent advocates as 20 per cent and our mortality rate has been 15 per cent. On the other hand, it is claimed by many that the unhooking of the gastro-enterostomy and restoration of the digestive stream is frequently followed by a recurrence of the original ulcer and such has been our experience—40 per cent recurrent duodenal ulcer in such procedures.

There are certain basic facts which must be admitted in any discussion of the surgical treatment of peptic ulcer. It must be admitted that both physicians and patients have accepted and do accept the original peptic ulcer with all too great complacency. The mortality from hemorrhage alone in this group of patients while in our hands in the hospital has been 5 per cent, 1 in every 20 patients. It must be admitted that gastro-



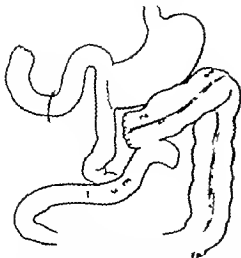


Fig. 6 This drawing diagrammatically illustrates the ideal procedure for gastrojejunocolic fistula. Resection of the stomach including the old gastro-enterostomy and the gastrojejunal ulcer, resection of the portion of the jejunum containing the ulcer and to end anastomosis of the jejunum, resection of the ascending colon, hepatic flexure, and portion of the transverse colon beyond the fistula and anastomosis of the jejunum to the cut end of the stomach and anastomosis of the jejunum to the cut end of the transverse colon. This, unfortunately is too much surgery for many of the patients with gastrojejunocolic fistulae to endure. Up to the present it is, however, the only plan whereby one may remove the large gastro-jejuno-colic fistulae without contamination of the peritoneum by colon contents. It must be understood that this discussion does not include the small gastrojejunocolic fistulae which can usually be handled quite satisfactorily by separation and severance.

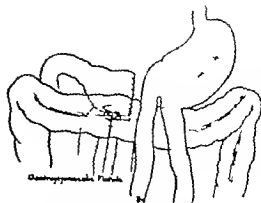


Fig. 7 This drawing illustrates the procedure described in the text which we have twice employed. Through left rectus incision, the stomach is cut off proximal to the ulcerated stomach and fistula and the jejunum beyond the gastro-enterostomy anastomosis to the cut end of the stomach. In both of these cases operations were immediately successful but ultimately (30 days and 3 months) the patients died of conditions, one coronary disease and one untreated intestinal obstruction, not directly related to the procedure. This plan may still prove useful procedure in dividing the radical removal of stomach, colon, and jejunum in the large gastrojejunocolic fistulae into less shocking two stage procedure. It was hoped that by subtracting gastric contents by this procedure, closure of the ulcer and lessening of the induration about the fistula might occur. Autopsy in both of these cases, in one 30 days after operation and the other 3 months after operation showed the induration to be still marked and the ulcer unhealed. Should we employ the procedure again, we would, we believe, remove the lower end of the stomach, jejunum and right colon through right rectus incision at the end of 3 weeks.

enterostomy is not a desirable type of operative procedure to be routinely applied to the surgical treatment of peptic ulcer as it has been in past years. It must be admitted that pyloroplasty (the safest of all operations for ulcer) is difficult to apply in many of the patients with duodenal ulcer due to the scarring and distortion of the duodenum by the ulcer. It must be admitted that radical partial gastrectomy gives the highest percentages of complete and permanent relief from ulcer symptoms and the lowest percentage of recurrent anastomatic ulcers, but it must also be frankly admitted that it has and probably always will have a mortality rate except in selected cases which both to the patient and surgeon is disturbing.

It must be admitted that while we can by operative procedures handle small gastro-

jejuno-colic fistulas with reasonable satisfaction we are faced with a situation which at least in our hands has up to the present proved almost insurmountable when the fistulous opening into the transverse colon in gastrojejuno-colic fistula is a large one for example the size of a quarter half-dollar or dollar (Fig. 5) as it so often is.

In operating upon such large fistulas between the colon stomach and jejunum, one is faced with the dilemma of producing peritoneal contamination with colonic contents on separating the large fistula with the need of trying to close a fistulous opening into the colon when that structure is badly indurated and so holds stitches badly or with the necessity of doing a block removal of stomach, jejunum, and midcolon which necessitates three resections at one sitting, resection of the

stomach jejunum and transverse colon (Fig 6) We have successfully accomplished this but it is a procedure of too great magnitude to be routinely applicable to this condition with a reasonable mortality We have employed numerous procedures in an attempt to decrease the danger and mortality in these trying cases Twice we have cut the stomach across proximal to the old anastomosis and so proximal to the gastrojejuno-colic fistula have closed the distal end and anastomosed a segment of jejunum by the Polya method distal to the fistulous connection between the stomach, jejunum and colon We have hoped by this procedure to cause the ingested food to pass directly into the jejunum beyond the old gastrojejunostomy and beyond the fistulous opening into the colon (Fig 7), thus segregating the section of stomach and jejunum containing the ulcer and also segregating the fistula By this plan it was hoped that food would be absorbed and utilized as it passed along the jejunum and not through the fistulous opening into the transverse colon, resulting as it has in some of the cases in a weight loss of several pounds a week

Both patients made excellent operative recoveries but one died a cardiac death 26 days after operation when ready to go home and the other died of intestinal obstruction 6 months after leaving the hospital We must admit that when we are faced with a patient with a gastrojejunal ulcer which has perforated into the transverse colon, and produced a gastrojejuno-colic fistula of large caliber and surrounded, as they always are, by a large area of induration, see Figure 5, we are still considerably at a loss as to how it can be surgically cared for with reasonable safety

We must admit finally, we think, and most importantly that most patients are not aware of how unsatisfactory the situation is as relates to the surgery of peptic ulcer and so do not feel as strongly as they should about the compelling need for modification of living, eating, smoking, and drinking habits, in order that they may avoid the necessity of facing an unsatisfactory surgical procedure or a satisfactory one with an unsatisfactory risk rate One of us (FHL) is self-conscious of having harped upon this aspect of the ulcer

situation but nevertheless feels it his duty again to repeat that unless patients with a peptic ulcer are frankly told of this list of admissions and are not permitted to assume that the operation which they accept is an entirely satisfactory one, then how can they ever be made to take their responsibility seriously or finally as they all eventually must?

#### SUMMARY AND CONCLUSIONS

The literature has been reviewed from the date of the paper by the author and Dr Jordan, 1928 to July, 1934 The number of reported anastomotic ulcers is recorded The variation in percentages of anastomotic ulcer in gastro enterostomy and resection is also recorded

Excerpts from the writings of authors interested in this subject are quoted to show the wide range of opinions held by experienced surgeons regarding this subject both as relates to its origin and incidence

As the result of this and our earlier (1928) review of the literature together with our experience, it is our conviction that gastro-enterostomy is not an operation that should be routinely utilized for peptic, particularly duodenal, ulcer

Some of the facts which predispose to the occurrence of gastrojejunal ulcer are recorded

A list of disturbing admissions regarding the surgery of peptic ulcer is frankly recorded This is done with no purpose of being destructively critical but rather that they may be unhesitatingly faced and we again repeat that unless patients are freely told of these disturbing admissions how can they ever be made to comprehend their responsibility seriously before or after operation, accept it finally, and live accordingly as they all eventually do in such other diseases as tuberculosis, pernicious anemia, and diabetes?

#### BIBLIOGRAPHY

- 1 ALLEN, N M. *Am. J Surg*, 1928, 5 128, *J Michigan Med Soc.*, 1931, 30 496
- 2 ANDREWS. *Surg Clin N America*, 1933, 13 1201
- 3 BAGER, B. *Acta. chirurg Scand*, 1929, 64 Suppl 11
- 4 BALFOUR, D C. *Ann Surg* 1928, 88 548, *Ann. Surg*, 1929, 90 535, *Surg Clin N America*, 1929, 9 23, *Ann. Surg*, 1930, 92, 558, *Proceed Mayo Clin*, 1932, 7 189
- 5 BENEDICT, E B. *Surg, Gynec. & Obst.*, 1933, 56 807

6. BIERO, A. A. *Ann. Surg.* 1930, 90 340
7. BRIDGEMAN, P. *Lyon chir.* 1911, 89 577
8. BLOCH, L. J. *Am. M. Ass.*, 1934, 95 883
9. BRANTZ, J. *Bull. et Mém. Soc. nat. de chir.* 1912, 25. 871
10. BRANTZ, C. E. and BOYER, W. *Deutsche Zeitschr. f. Chir.* 1912, 276 93
11. BROOKLYN L. Guy's Hospital Rep. 1930, 80 297
12. BROOKS, Brit. M. J. 1910, 786
13. BUCKSTEIN, J. *Am. J. Roentgenol.*, 1912, 27 30
14. BUDOW, W. *Arch. f. Klin. Chir.* 1928, 121 600
15. CANOT CHIR. *New England J. Med.* 1920, 307 382
16. CAMP, J. D. *Med. Clin. N. America*, 1934, 14 707
17. CALLOT, A. *Polichin.* 1912, 301 666
18. CHANDLER. *Arch. de mal. de l'appar. digest.* 1912, 1902
19. CLAY, C. *Rev. de chir. Par.* 1912, 51 807
20. DAVENPORT, C. B. J. *Am. M. Ass.*, 93 97 99
21. DRAVER, J. B. *Atlantic M. J.* 1921, 3 708
22. DOUGLAS, J. T. *Am. Surg.*, 1930, vol. 41
23. DOWN, H. I. *Proc. Staff Meet. Mayo Clin.*, 93 6-803
24. FREELING, W. W. *Ann. Surg.* 1912, 97 417
25. FRIEDBERG, S. P. J. *Am. M. Ass.*, 1928, 90 870
26. ELANKY, N. M. *Arch. f. Klin. Chir.* 1929, 98 5
27. ELLIS, W. L., Jr. *Ann. Surg.* 1911, 98-99
28. ELLERMAN, G. B. *Med. Clin. N. America*, 1912, 1 371
29. FERRY, J. M. T. and HARRIS, E. M. Jr. *Ann. Surg.* 1926, 90 904
30. FRIEDBERG, H. *Surg. Gynec. & Obst.* 1913 5 1099
31. FUCHS, A. *Zentralbl. f. Chir.* 1912, 20 700
32. FURMAN-SMITH, M. and McIVER, M. A. *Am. J. M. Sc.* 1926, 177 11
33. FREEDMAN, J. O. T. *Ann. Surg.* 1930, 93 48 409
34. FROST, A. *Brit. M. J.* 1929, 147 11
35. GUTHRIE, T. *Am. Surg.* 1930, 48 43
36. GOWAT, A. J. *de chir.* 1911, 18 40
37. GRAY, RONALD R. *Gastrointestinal and rectal ulcers*. Not yet published. Read at last meeting of the American Medical Association.
38. HARRIS, von H. *Zentralbl. f. Chir.*, 1930, 57 66
39. HARRIS, F. R. *Surg. Clin. N. America*, 1911, 3 843
40. HARTWELL, J. A. and FELTZ, R. K. T. *Am. Surg.* 1930, 48
41. HAYES. *Ann. Surg.* 1929, 91 601 (Part Thoms, 1929)
42. HENSON, J. W. *Surg. Clin. N. America*, 1911, 697
43. IDEM. *Am. J. Surg.* 1912, 80 107
44. HENSON, J. WILLIAM, and CHURCH, RICHARD E. The incidence of gastrojejunal ulcer following gastroenterostomy. *Am. J. Digest. Dis. & Nutrition*, 1934, 320
45. HOSLEY, J. S. T. *Am. Surg.* 1930, 48 33
46. HUBB, A. F. and COHEN, C. F. *Proc. Roy. Soc. Med.* 1931, 24 797
47. HUBB, A. F. and STEWART, M. J. *Lancet*, 1931, 743, 805
48. JONES, T. E. *Guy's Hosp. Rep.* 1918, 38 51
49. JONES, S. *Bull. et Mém. Soc. nat. de chir.* 1930, 23 33
50. JONES, J. *de chir.* 1911, 18
51. JONES, E. *Wien. klin. Wochenschr.* 1929, 48 300
52. KATZ, E. D. *Surg. Clin. N. America*, 1931, 687
53. KLEIN. *Ann. Surg.* 1929, 90 63
54. KOSCHETZKY, G. E. *Engel. d. med. Med. Kinderh.* 1930, 37 24
55. LARSON, O. F. *Surg. Clin. N. America*, 1911, 13 47
56. LEPLAT. *Bull. et Mém. Soc. de chir. de Par.* 1921, 20 466
57. LEROUX, R. *Bull. et Mém. Soc. nat. de chir.* 1920, 23 518
58. LEVINE, J. PIERCE, F. D. and BRADY, A. J. J. *Chir. Invert.*, 1912, 15
59. LEWIS, R. *Ann. Surg.* 1929, 91 520
60. LINCOLN, A. and WOLFE, *Surg. Gynec. & Obst.*, 1911, 21 611
61. LORING, H. W. *Surg. Gynec. & Obst.*, 1928, 47 403
62. LOTT, A. F. *Brit. M. J.* 1929, 147 974
63. MACGILLIVRAY. *Ann. Surg.* 1912, 97 34
64. MARSH, M. *Brit. M. J.* 1924, 59 61
65. MALLORY, G. P. *Lyon med.* 1933, 51 193
66. MARTELL, E. *Lyon chir.* 1912, 20 64
67. MEYER, K. A. and ROSE, P. A. *Surg. Clin. N. Amer.* 1912, 3 51
68. MILLER, J. R., and HOLLAND, W. H. *Rhine M. J.* 1911, 41 487
69. MORTON, C. B. and GRAM, J. R. *Ann. Surg.* 1929, 93 73
70. MORTIMER, R. *Brit. M. J.* 1928, 2 1001
71. NEUBER, G. *Deutsche Zeitschr. f. Chir.*, 1929, 112 149
72. NIXON, P. L., and LOWRY, S. T. *Med. J. & Rec.*, 1924, 28 584
73. NYSTROM, G. and SODERBERG, F. *Zentralbl. f. Chir.* 1912, 25 50
74. NYSTROM, O. T. *Am. Surg.* 1930, 48 76
75. OBERHOLZER, A. and STARTZ, E. *Deutsche Zeitschr. f. Chir.* 1912, 14 387
76. OGDON, BERT. *Proc. Soc. Expt. Med. & Med.* 1931, 20 835
77. POINDEXTE, W. *Zentralbl. f. Chir.*, 1912, 25 1700
78. RAUER, H. *Deutsche Zeitschr. f. Chir.* 1912, 24 20
79. ROBINSON, V. P. *Lancet*, 1928, 701
80. ROBINSON, E. W. *Am. Surg.* 1930, 91
81. SCHWARTZ, E. *Theor. d. Chir.* 1928, 69 17
82. IDEM. *Arch. f. Klin. Chir.* 1928, 51 445
83. SCHWARTZ, F. *Brit. M. J.* 1929, 47 126
84. SCOTT, W. J. M. *Arch. Surg.* 1930, 12 584
85. SEVER, P. *Ann. Chir.* 1929, 1007
86. SOLZ, R. *Engel. d. med.* 1929, 776
87. STANBROOK, F. *Wien. klin. Wochenschr.* 1929, 21 904, *Arch. f. Klin. Chir.* 1929, 124 164, *Engel. d. Chir. Orthop.*, 1931, 5 380
88. STEINER, E. *Deutsche Zeitschr. f. Chir.* 1911, 13 404
89. STEINBERG, M. E. *Am. J. Surg.* 1934, 12 157
90. STONE, J. E. *Am. J. Surg.* 1912, 240
91. ST. JOHN, F. R. *Ann. Surg.*, 1930, 91 507
92. STRAUSS, A. J. *Am. M. Ass.*, 1928, 90 81
93. THOMPSON, W. and STEWART, M. J. *Brit. J. Surg.* 1928, 3 17
94. THOMAS, T. *Orth. Chir.* 1929, 43
95. VALBORE, Polichin. 1912, 30 444
96. VILLARD, R. *Bull. d. M. med. Bologna*, 1911, 103 21
97. WALLON, A. J. *Textbook of Surgical Dyspepsia*, 1930, Brit. J. Surg., 1931, 21 11
98. WALTON, F. *Zentralbl. f. Chir.* 1931, 58 2679
99. WELLS, J. F. *Am. J. Surg.*, 1929, 7 905
100. WELLS, D. P. D. *Ann. Surg.*, 1934, 99 402
101. WILLIS, P. W. *Surg. Clin. N. America*, 1912, 13 13
102. WOODRIDGE, C. J. A. *Brit. M. J.* 1929, 1 667
103. ZUCKERWALD, L. and FETZ, T. *Deutsche Zeitschr. f. Chir.* 1911, 31 79

# HOITINK TREATMENT OF ACUTE FATAL HEMORRHAGE

## TREATMENT OF ACUTE FATAL HEMORRHAGE BY INJECTION OF ARTIFICIAL BLOOD SUBSTITUTES<sup>1</sup>

### A COMPARATIVE STUDY OF ARTIFICIAL BLOOD SUBSTITUTES

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ONE would seem to be behind the times if today he attempted to save an exsanguinated patient by some means other than by blood transfusion. If we study the literature on blood transfusion it is apparent that in numerous cases blood transfusion has saved life after great hemorrhage. It is true however, that this operation may not be entirely without danger, for often there may be injurious consequences, sometimes even death.

It is not surprising that these disagreeable experiences with blood transfusion occur, for in performing a blood transfusion operation, we inflict a very complicated system, the blood of the donor, upon another equally complicated system, the blood of the recipient, and these two systems possess a certain degree of individuality.

Blood testing to determine types and quality of blood at best gives only an imperfect idea of the real properties of the bloods which are to be mixed. If one reflects a moment about the numerous known, but more especially the unknown, properties of blood in their infinitely changing individual characteristics, blood transfusion at present can only be called a "dark" operation, as we do not know exactly what is put into the blood circulation of the recipient and what will be the consequences. This is a great disadvantage and justifies the seeking for other means of treating acute fatal hemorrhage.

For about 50 years infusion was considered the method of choice in the treatment of great losses of blood, artificially prepared fluids (artificial blood substitutes) were infused or injected in an effort to avert fatal consequences in great blood loss. At first sodium chloride solution was the principal solution used. Gradually, however, it was supplanted by other fluids which were expected to give

better reactions.<sup>2</sup> Treatment by infusion was thrown into the background however, when the introduction of the blood of donor to recipient was considered to be the only right method to use. As the use of blood transfusion has become more extensive, difficulties have been encountered and as there are still obstacles to overcome the investigation of the other methods of treating considerable blood loss should be continued.

#### EXPERIMENTAL DATA

Therefore I began the study of artificial blood substitutes, the injection of which—if they proved to be valuable in an acute hemorrhage—would as a rule have in addition the advantage of surpassing blood transfusion in so far as the treatment might be more quickly accomplished.

The life saving actions of several artificial blood substitutes were compared. For this purpose a large quantity of blood was taken from dogs by allowing the blood to flow from the carotid artery through a cannula, and shortly afterward injecting the substitute into the external jugular vein. The immediate reaction was determined as well as the late recovery of the animal. Much attention was paid to the question as to how far the bleeding should be carried in order to determine the comparative values of the substitutes as to their life saving actions. It seems to me that the methods generally used to obtain equal losses of blood are inadequate, I believe that we must determine rather what effect the loss of a certain amount of blood will have on the animal in question.

Judgment as to the seriousness of a hemorrhage must be based on the reaction of the animal to the loss of blood, from the symptoms.

<sup>1</sup>See the extensive "Historical review of the development of substitution of blood by means of artificial substitutes, in my thesis, pp. 175 to 235.

<sup>2</sup>The results of my research were extensively described in my book entitled "Vergelykend onderzoek over de werking van verschillende kunstmatige bloedvervangmiddelen by levensgevaarlijke bloedverliezen." Theses de doct. Utrecht Holland Feb. 1934.

which the animal itself shows during the increasing loss of blood we must try to ascertain the degrees of artificial anemia in their biological significance as applied to the animal in question.

My study of the action of blood substitutes has proved that we must stop bleeding the animal at an accurately determined moment at which (a) the loss of blood would certainly prove fatal without the infusion (b) the anemia has an equivalent "biological value" in each separate animal used.

I found that to determine this moment attention must be directed especially to (1) the symptoms shown by breathing (a) the peculiarities of the pulse—tactile\* observation on the femoral artery and visual pulse control by observing the stream of blood flowing from the artery (3) the appearance of convulsions.

Observation of respiration revealed four forms of breathing as the loss of blood increased—approximately the same as those described by E. Holovtshiner for rabbits in similar circumstances.

The convulsions noticed are, first extensor spasms of the paws, the presence of which proved to be of no practical value in estimating the grade of artificial anemia. Besides, "general extensor convulsions" were observed, by which is meant tonic spasms of the whole animal. During such spasms the paws are tensely stretched, the head and neck are extended far backward, and the back is bent in opisthotonus. It is this "general extensor spasm" which is of great importance in determining the moment at which the hemorrhage must be stopped.

By paying attention to each of the aforesaid symptoms separately however it appeared to be impossible to determine sufficiently accurately the moment at which the loss of blood should cease, if the two demands mentioned were to be complied with. However by experiments, a complex of symptoms was evolved by observing as a whole, the convulsions, the respiration and the peculiarities of the stream of blood together.

It appeared that the three symptoms to be mentioned each one of which by itself may be an important indicator of the degree of

anemia show themselves almost simultaneously as in a "snapshot," the general spasm being the one to produce the effect of suddenness. The moment at which these symptoms show themselves in their peculiar composition can be accurately determined, and is thus of practical use in pointing out when the bleeding should be stopped. The three symptoms are (a) the sudden appearance of a general extensor spasm extensor convulsions of the paws having been noticed before at different periods (b) the sudden stopping of flow or dripping of blood for a moment, to continue again or else to stop entirely (c) the end of the syncope form of breathing that is, the animal breathes only superficially and very irregularly only a few breaths are taken or the respiration ceases altogether.

From the curious coincidence of these three important symptoms, I thought I could draw the conclusion that the loss of blood had passed a certain threshold determined by the animal itself and had attained critical proportions. I could demonstrate that such a loss of blood was fatal for the animal.

By continually increasing the bleeding until there is visible the triad of symptoms of functional fatal hemorrhage, which may be accurately observed it was possible in several animals, to cause fatal hemorrhages all of which are biologically equivalent.<sup>1</sup>

It was now possible to compare with sufficient accuracy the action of different substitutes for blood when given to different animals.

The characteristic symptoms of functional fatal hemorrhage appeared when on an average 56 to 57 cubic centimeters of blood per kilogram of body weight had been lost. The smallest loss of blood at which the symptoms appeared was 50 cubic centimeters and the largest 64 cubic centimeters per kilogram of body weight.

Hemorrhage which is continued until marked irregular syncope respiration is seen is also considered fatal for dogs. Though experiments in which the animals have been bled to this extent cannot be included when

<sup>1</sup>By functional fatal hemorrhage I mean that no such damage has been done to the animal organism through the loss of blood that its functions are very greatly hampered, while mechanical fatal hemorrhage simply means that no more blood can be abstracted from the animal.

TABLE I—BLEEDING AND SUBSEQUENT INJECTION OF SODIUM CHLORIDE SOLUTION INTO THE VENA JUGULARIS EXTERNA

Dog number	Sex age	Weight, kilograms	Loss of blood c. cm	Loss of blood per kilogram of body weight c. cm	Triad?	Quantity of substitute injected	Result of the injection	Anesthesia
11	♂ ± 5Y	~1.5	1200	56	No	960 c. cm. 0.7% Na Cl solution	Saved	Local
16	♀ ± 2Y	16.5	1050	64	Yes	840 c. cm. 0.9% Na Cl solution	Saved	Local
19	♀ 9210Y	23	1200	52	Yes	960 c. cm. 0.9% Na Cl solution	Saved	Local
29	♂ ± 5Y	14.5	800	55		640 c. cm. 0.9% Na Cl solution	Saved	Local†
24	♀ ± 3Y	17.5	1100	63	Yes	860 c. cm. 0.9% Na Cl solution	Saved	Local
27	♂ ± 6Y	27	1200	44	No	960 c. cm. 0.9% Na Cl solution	Saved	540 m gr morphin† subcutaneous

\*Makes the impression after the bleeding of being dead

†Bleeding was probably extended beyond the appearance of the triad. This dog had diseased kidneys before the operation.

‡About 6 weeks before this dog suffered a hemorrhage of 55 c. cm per kilogram of body weight, after which chlorides-Normet were injected with good result.

comparing the substitutes for blood, they can give us information as to the latter's power to save life

In accordance with the principles outlined, I examined in acute fatal hemorrhage, the action of sodium chloride solution 0.7 and 0.9 per cent, Ringer's fluid<sup>1</sup> (0.95 per cent NaCl, 0.02 per cent KCl, 0.02 per cent CaCl<sub>2</sub>), Locke-Ringer (0.9 per cent NaCl, 0.024 per cent CaCl<sub>2</sub>, 0.042 per cent KCl, 0.1 per cent glucose, 0.02 per cent NaHCO<sub>3</sub>, saturated with oxygen), Tyrode (0.8 per cent NaCl, 0.02 per cent KCl, 0.02 per cent CaCl<sub>2</sub>, 0.01 per cent MgCl<sub>2</sub>, 0.005 per cent NaH<sub>2</sub>PO<sub>4</sub>, 0.1 per cent NaHCO<sub>3</sub>, 0.1 per cent glucose), normosal, tutofusin (these two fluids are modern substitutes, prepared in a factory, the composition is kept a secret, but is very much like Tyrode's fluid), and sérum Normet chirurgical

Sérum Normet is a citrate solution, used by L. Normet<sup>2</sup> and is based on his investigations on the therapeutic activity of citrates. Normet's solution consists of 22 grams of sodium citrate, 6.50 grams of neutral calcium citrate, 4.50 grams of neutral magnesium citrate, 1 gram of iron ammonium citrate, 0.15 gram of manganese citrate, distilled water to 1000 cubic centimeters. Twenty cubic centimeters of this solution are added to 1000 cubic centimeters of sodium chloride solution 0.7 per cent. The liquid thus obtained can be used

as a blood substitute and for that purpose is injected into the circulation up to the equivalent of two-thirds to four-fifths of the amount of blood lost

Normet claimed that the citrate solution he used as a blood substitute not only had a better immediate action, but also a peculiar, stimulating influence on the restoration of the blood. The favorable action which Normet claimed for the sérum Normet he ascribed to the fact that the metals in the fluid were present as citrates

In order to determine whether a possibly more favorable action of the sérum Normet in acute profuse hemorrhages is due to the fact that the metals used are combined with citric acid, I made a solution that contained the metals in the sérum Normet but used chlorides in equivalent quantities (chlorides Normet). A comparison was made of the effects of sérum Normet and chlorides Normet

Water was also once injected

The results of my experiments on the life saving action of the various substitutes are given in Tables I to IV

As it was only later on in our study that a clear cut image of the symptoms of fatal hemorrhage was formed, these symptoms were not noticed in a number of dogs in the early experiments. The greater number of the animals, however, suffered a fatal loss of blood so that conclusions can be reached as to the life saving action of the fluid in question. For a comparison of the value of the various infusion liquids we can make use

<sup>1</sup>The methods of preparing the different fluids are mentioned in full in my thesis

<sup>2</sup>A. W. J. H. Hoitink, thesis pages 226-234, contains a summary of Normet's work and of the literature on his fluids

TABLE II—BLEEDING AND SUBSEQUENT INJECTION INTO THE VENA JUGULARIS EXTERNA OF MORE COMPLICATED SOLUTIONS VIZ., RINGER'S FLUID LOCKE-RINGER AND TYRODE SOLUTIONS NORMAL AND TUDOFUSIN

Day number	Sex, age	Weight, kilograms	Loss of blood, c. cm.	Loss of blood per kilogram of body weight, cm.	Triad*	Quantity of substitute injected, c. cm.	Result of the injection	Anesthesia
1	♀ 2 yr	20	200	10	No	200 cc. of Ringer's fluid	Died 7 hours after injection	250 cc. of morphine subcutaneous, supported by ether narcosis
7	♀ 2 yr	16	300	18	No	600 cc. of Locke-Ringer fluid	Survived	Local†
	♀ 115	5	770	47	No	600 c. cm. Locke-Ringer	Survived	Local‡
8	♂ 6y	24	600	25	Yes	770 c. cm. Tyrode	Survived	Local
	♂ 11.7	25.5	11.00	43	Yes	20 cc. normal	Survived	Local
11	♀ 2 yr	16.5	20	12	Bleeding continued beyond triad	600 cc. Tudofusin	Died	Local

\*Doubtful if this loss of blood is certainly fatal.

†Maintaining the appearance after the bleeding of being dead.

‡Not dead after operation in power condition.

§Unsettled, in both the triad showed small after comparatively slight loss of blood.

TABLE III—BLEEDING AND SUBSEQUENT INJECTION OF SERUM NORMET CHIRURGICAL INTO THE VENA JUGULARIS EXTERNA

Day number	Sex, age	Weight, kilograms	Loss of blood, cm.	Loss of blood per kilogram of body weight, c. cm.	Triad†	Quantity of substitute injected, c. cm.	Result of the injection	Anesthesia
	♂ 2.77	20	870	43	No	775	Survived	Local‡
	♂ 2.77	24	800	33	No	875	Survived	250 cc. of morphine subcutaneous
	♂ 2.77	20.75	600	28	No	600	Survived	200 cc. of morphine subcutaneous
	♂ 2.49	27	1,120	41	No	20	Survived	Local supported by ether narcosis
	♂ 3	20	1000	50	No	800	Survived	Local
14	♂ 2.157		200	30	No	600	Survived	Local
17	♀ 2.20	15	2000	133	Yes	675	Survived	Local
20	♂ 4.17	24	200	30	Yes	200	Survived	Local
20	♂ 2.94	20.5	1500	73	Yes	670	Survived	Local

\*Doubtful if this loss of blood is certainly fatal. Splenic vein severed some minutes before.

†The blood condition directly after operation.

‡Five days after operation, been good (subnormal) lost in weight.

§Five days after operation, kidneys below the operation.

only of the experiments in which the bleeding was stopped as soon as the triad made its appearance. Such experiments are indicated in the tables.

In surveying the results of our study it was found that all substitutes had the ability to save life after biologically equivalent fatal hemorrhages. It is not surprising that the

dog that received an injection of Ringer solution died (Table II) if attention is drawn to a few details. After general anesthesia by means of a heavy dose of morphine supplemented with ether narcotics this dog was fatally bled. In addition to these two factors harmful to recovery after hemorrhage the pathologist found at postmortem examination that the dog had been suffering from cancer. Moreover peculiar tumors were found in the spleen (multiple splenotolliculomas). In the

The dog which, after loss of blood of 100 cc. in 10 minutes (see table) died, was per-  
 mitted to recover after the injection of 200 cc. of Ringer's solution. The dog, however, died about 10 minutes after the injection.

TABLE IV—BLEEDING AND SUBSEQUENT INJECTION OF "CHLORIDES NORMET" INTO THE VENA JUGULARIS EXTERNA

Dog number	Sex, age	Weight, kilograms	Loss of blood, c. cm	Loss of blood per kilogram of body weight, c. cm	Triad?	Quantity of substitute injected, c. cm	Result of the injection	Anesthesia
23	♂ 4½y	25	1375	55	Yes	1100	Saved	Local*
27	♂ ± 6y	24.5	1350	55	Yes	1080	Saved	Local†

\*After operation this dog got diseased kidneys, urine also showed reduction (Makes the impression after the bleeding of being dead.)

†After operation a few abnormalities in urine, also reduction

tumors and the surrounding tissue much blood was found, at a distance from the tumors the splenic tissue was conspicuously poor in blood. Therefore, I wondered if the spleen had been able to react sufficiently to offset the loss of blood, as described by J Barcroft. It seemed to me quite possible that this diseased spleen in addition to an insufficient power to swell, i.e., to stock blood, had been able to contract only imperfectly, so that the organism lacked an important means of defense against the consequences of acute loss of blood. If these factors all acting unfavorably are considered I think that the death of this dog should not be attributed to Ringer's solution.

The experiment in which tutofusin was injected does not give an idea as to the life saving action of this substitute, as the infusion was administered to an anemic dog and the bleeding was continued far beyond the appearance of the "triad."

If the fact that water is by no means harmless to the blood is considered, the result of the experiment with water is not astonishing, for in addition to the fatal loss of blood further damage was done by the destruction of a great number of the remaining blood cells, when a large quantity of water was so quickly injected into the blood.

Apart from these cases in which it is quite obvious that infusion could not save life, all substitutes for blood injected appeared to be life saving. That the more complicated substitutes produced better results than sodium chloride solution I could find no proof, on the contrary, ordinary sodium chloride solution was unsurpassed in saving the animals doomed to death by loss of blood.

As a rule the dogs recovered quickly after the injection of the various substitutes. The

defective respiration, which sometimes stopped entirely, showed quick improvement. Then there was a peculiar form of respiration characterized by a short, scarcely audible inspiration, followed by longer snuffing expiration. The sound thus produced reminded one of the noise made by a railway engine as it begins to move. I called this form of breathing the "engine respiration." It is especially remarkable that the expiration is predominant. It seems as if the organism uses this form of breathing to rid itself of injurious substances. After a short time the "engine respiration" changes again into usual breathing without an abnormal predominance in expiration. All other signs of returning life quickly appear after the infusion.

No real damage due to the infusion of substitutes was noticed except that in a few instances there were abnormalities in the urine for a short period<sup>1</sup> especially after infusion of chlorides Normet and sometimes after serum Normet. These abnormalities in the urine were not of a serious nature, however. In dogs which had distinctly diseased kidneys, no bad effect as far as the urine was concerned was observed after the injection of a 0.9 per cent sodium chloride solution and of serum Normet after hemorrhage.

In addition to the study of the life saving action of artificial blood substitutes, the following determinations as to the influence of the substitutes on the restoration of the blood were made: the number of erythrocytes per cubic millimeter, the hemoglobin percentage, the method of S. Y. Wong being used, the Sahli value, the average amount of hemoglobin of an erythrocyte, the number of reticulocytes, polychromatophilic erythrocytes.

<sup>1</sup>After hemorrhages without subsequent infusion we also find abnormalities in the urine of dogs, as is shown by this research and another we have taken in hand.



TABLE V

Injected fluid	Number of reticulocytes before operation	Direct count of reticulocytes after operation	Days after operation greatest number was observed	Ratio of blood per kilogram of body weight lost
Sodium chloride solution	2	46.5	6	25
Sodium chloride solution	2, 2	27		25
Sodium chloride solution	2	26	6	
Lactic Ringer		10 (and 14)	20 (and 22)	26
Tyrosine	2	27.6	6	26
Metacoll		22		26
Serum Normet		22		23
Serum Normet		20		24
Serum Normet	4	26		20
Serum Normet	7	26		20
Serum Normet	2, 2	26.8		22
Chlorides Normet		26	6	25
Chlorides Normet	4, 2	27 (and 17.5)	and 6	23
Hemoglobin extract prepared by centrifugation	8	20.4	6	22

normoblasts, red blood cells with Howell-Jolly particles and other nucleus particles basophilic erythrocytes form and size of the red blood cells other peculiarities of the red blood picture the number of leucocytes per cubic millimeter the relative number of the different sorts of leucocytes. Subsequently we examined the total proteins of the blood plasma, the albumin and globulin content the relative proportion of the albumins and globulins the non protein nitrogen content of the plasma. We tried especially to determine the magnitude of the restorative power of the solutions by comparing the number of reticulocytes before the hemorrhage and after the injection of the solution.

Table V gives an idea of the behavior of the reticulocytes after hemorrhage and subsequent injection of the various blood substitutes used by me.

If we assume that a comparison of the number of reticulocytes per 100 erythrocytes present during the restoration of the blood with the number before the hemorrhage is an indication of the magnitude of the restoration of the blood then my experiment would indi-

cate that the serum Normet did not have a distinct stimulating action on the hematopoietic organs. It goes without saying that here again the unknown peculiar restorative power of the animal in question makes an accurate comparison impossible. We may therefore, only venture an opinion as to the more or less favorable action of the substitutes used on the restoration of the blood as evidenced by the distinct differences in the number of reticulocytes. From the results shown in Table V it does not seem that a more favorable result is secured with serum Normet than with salt solution in restoring the blood. If we compare the number of reticulocytes before operation with the greatest number after the operation it is remarkable to note that when salt solution was used the largest number on an average was 14 times the normal number whereas in the experiments in which serum Normet was injected, the number on an average was only 3 times the normal.<sup>1</sup> These facts seem to speak rather in favor of the sodium chloride solution.

Not one of the substitutes used however showed an extraordinarily favorable influence on the restoration of the form elements, hemoglobin and proteins. No evidence was found to indicate a stimulating effect of the serum Normet on the hematopoietic organs.

In addition to these investigations, we made tests to determine how rapidly the urine and the sodium chloride were excreted after great loss of blood and subsequent infusion. These experiments showed that the organism which has lost most of its blood retains for some time the substitutes injected. I did not find any evidence of a quick excretion of the substitutes this is especially true of the sodium chloride solution I did find however that after infusion of a sodium chloride solution in a dog that had lost no blood an increased secretion of urine and sodium chloride started soon after the infusion.

Summarizing it appeared from my experiments that the artificial substitutes for blood injected into a vein after an acute profuse hemorrhage save life. A comparison of the merits of salt solution and other more compli-

<sup>1</sup>For the comparison with the Normet experiments only the results were used in which the loss of blood was about as large as in the other bloodless experiments.

cated manufactured substitutes showed that the latter brought about no more favorable action than the ordinary sodium chloride solution

Though we did not find any damage even at autopsy when a 0.7 per cent sodium chloride solution was used a 0.9 per cent solution is preferable, as evidenced by the experiments of H. J. Hamburger

#### DISCUSSION OF SEVERAL BLOOD SUBSTITUTES

With my results as a basis and after an extensive study of the literature on the infusion liquids I have attempted to criticize the artificial blood substitutes as to their worth in acute fatal hemorrhage. Some of the solutions most commonly used will be discussed briefly (17)

1 *Physiologically equilibrated solutions* As appears from my experiments these solutions show no better effect than the 0.9 per cent solution of sodium chloride. One great disadvantage in using the more complicated solutions is that it is very difficult to prepare them in a perfectly sterile manner without damaging their composition. In the modern preparation made in factories—normosal, tutofusin—this difficulty was not removed. Here we refer to A. Beck and also to W. Weichardt and H. Unger, who in 1928 and 1929 described the great dangers which may be attached to the injection of these liquids as a result of their not being quite sterile.

2 *Colloid infusion fluids* Best known is W. M. Bayliss' (5) solution consisting of 7 per cent gum arabic dissolved in 0.9 per cent sodium chloride solution. The addition was said to keep the liquid in the blood vessels for it was thought that the non-colloid liquids after infusion into the circulation disappeared from it very quickly. But this is by no means certain. The so called dilution tests by which certain elements in the blood are estimated before and after infusion, are valueless as far as determining the amount of infusion fluid circulating in the blood stream. It is especially from the varying number of erythrocytes per cubic millimeter that calculation is made as to the rapidity with which the injected fluids disappear from the circulation. However, six

factors are to be kept in mind in estimating the number of erythrocytes per cubic millimeter after hemorrhage and subsequent infusion, viz: (a) the quantity of blood remaining in the circulation, (b) the quantity of infusion fluid still in the blood vessels, (c) the tissue fluid which flows into the circulation, (d) the quantity of blood which proceeds from the spleen and which has a different composition to that already in the circulation, (e) the blood which is recruited from other blood stores, (f) the number of red blood cells damaged by the injection.

To draw a conclusion from the number of red blood cells per cubic millimeter as to the disappearance of the injected fluid from the circulation (which is, after all, only one of the many processes which take place) seems to me to be entirely arbitrary and not permissible. These same scruples exist when trying to obtain an impression of the rate of disappearance of the fluids by calculating the rise or fall of the hemoglobin or of the protein content of the plasma. If we use the proteins as an indicator, we must take the possibility into consideration that the walls of the blood vessels may be permeable for these substances in both directions. Also in determining the hematocrit—which is an unreliable method itself—the factors mentioned exercise their influence.

Moreover, the hemoglobin content did not always rise or fall with the number of red blood cells per cubic millimeter. The man who makes use of the erythrocyte count must get other results from his "dilution tests" than he who uses the hemoglobin content.

The colloid infusion fluids have no more favorable action than the fluids I used in my experiments. Barthélémy (5), by means of the Bayliss gum salt solution, could save dogs from which 60 to 70 per cent of the blood had been taken. If the hemorrhage was extended farther, the solution proved to be ineffective in saving life. The loss of blood in the experiments of Barthélémy was about as great as those in my dogs and the animals were saved by non-colloid fluids. I must also mention that the literature repeatedly describes dangers which may follow the injection of gum salt solutions. *The Journal of the American*

*Medical Association* (12) even warned against the gum salt solutions in an editorial.

At the end of this article I shall call attention to a theoretically construed disadvantage of the colloid fluid.

3. *Serum Normet* On the basis of our tests we could not discover any particularly favorable action of serum Normet over sodium chloride solution. Moreover as J. Giraud and P. Silhol (13) and E. Bressot (11) observed dangerous complications after the injection of this fluid—one of my observations also tends in this direction (16)—the use of serum Normet cannot be recommended.

4. *Isotonic sugar solutions* As far as I can learn isotonic sugar solutions, as blood substitutes, have never been proved to give better results than sodium chloride solutions. I believe that they have one disadvantage and that is that especially if they are kept in stock for some time the chance of alterations in the composition is greater. Then, too, it does not seem to me to be good practice to inject sugar into the circulation in the usual quantities, for a very unnatural hyperglycemia is caused which certainly has its disadvantages.

By making the infusion liquid isotonic by means of sodium chloride a solution is formed which is more akin to blood.

5. *Hypertonic (sugar) solutions* Especially E. Simenauer tried to draw the tissue fluid to the vessels by injecting a small quantity of a hypertonic glucose solution into the circulation (40 per cent invert sugar solution, known as shock calorose of which 30 cubic centimeters is to be injected). This method of treatment does not seem to me quite the right one in acute heavy hemorrhage. An attempt is made to draw the tissue fluid more quickly to the vessels but the injection into the vessels of the necessary fluid acts more quickly and better answers the purpose. Besides, the dehydration of tissues of the whole body is thus overcome.

6. *Blood transfusion* In my experiments, in which the bleeding was as extensive as possible, I was quite successful in substituting for the lost blood liquids that did not contain red blood cells or blood serum. It is apparent that it is not necessary to infuse strange blood in acute dangerous hemorrhages. I would point

out again that the great dangers connected with blood transfusion have influenced me in the conclusion that the prevailing opinion that hemorrhage calls for transfusion broadly speaking is not right.

7. *Sodium chloride solution.* On the basis of my own experiments, complemented by the facts found in the literature, I have come to the conclusion that in acute fatal hemorrhages the injection into a vein of 0.9 per cent sodium chloride solution is preferable to the injection of the other artificial blood substitutes and to blood transfusion! The objections to sodium chloride solution I have discussed in my thesis and I have tried to confute them.

My opinion is that for medical practice the 0.9 per cent sodium chloride solution is a blood substitute which can be prepared at any place and at any moment, is easily administered and has an excellent action. Elsewhere I have tried to explain the advantages of sodium chloride solution theoretically (16) I shall summarize very briefly.

1. In the treatment of acute dangerous hemorrhage the most urgent demand is a quick replenishing of the fluid of the vessels, so that the circulation can continue (F. Goltz) and the organism striving for recovery is helped past a dead-lock.

2. The various substitutes act, as to the propulsion of the contents of the vessels, in accordance with their volume. The water which all infusion fluids have in common, and which gives them volume stamps them as good substitutes. Mere water cannot be used for the injection into the circulation. However if water is rendered tolerable to the body by adding sodium chloride to it, it is an excellent blood substitute. Of the other additions no particular favorable action is seen in the infusion experiments. We have already pointed out that there are practical disadvantages.

3. The unphysiological fluid injected into the blood (e.g. sodium chloride solution) is

As to chronic loss of blood and the pre-attached waste hemorrhages, we also speak in this manner of a definite method of treatment can be resorted to in the first. However, I draw attention to the observations of P. J. Best, V. J. Reid, W. W. White, and C. C. Channing. They thought that they noticed a constriction of the blood vessels after infusion of sodium chloride solution by which stanching of blood was said to be effected. If these observations are correct, the infusion of sodium chloride solutions can also be of service in such clinically feared hemorrhages.

turned into a more physiological one after some time. For not only do we inject the substitute into the circulation itself but we introduce it into the whole quantity of fluid the body possesses because a constant exchange is taking place between the different fluids until the physiological margin is reached. That the organism with its large store of "physiological" fluid is easily able to neutralize the slight change into an "unphysiological" direction, is proved by the good results of the numerous (sodium chloride) infusions.

4 We put the least possible obstacles in the way of this turning of the fluid in the circulation to a physiological solution if we administer as a blood substitute water that is rendered harmless in the most simple way by the addition of sodium chloride. I consider the fact that it is easily movable an advantage. The great mobility of the liquid is a better guarantee of the quick issue of exchange that takes place to accomplish the "physiological balance" in regard to the composition of the fluid in the entire body. Therefore it seems to me biologically incorrect to use great effort to retain all the fluid injected in the circulation, as for instance when colloid infusion liquids are used. The loss of fluid suffered by the whole organism after a great hemorrhage is also fought more efficaciously by "movable" infusion liquids.

5 In acute dangerous hemorrhages the supply of blood from without the body is not necessary, sometimes dangerous.

Especially on these grounds I think I am able to support and to confirm the practical advantage of the 0.9 per cent sodium chloride solution.

As for the practical application of the 0.9 per cent sodium chloride solution, which we have given extensively elsewhere (17) we must remark that in acute fatal hemorrhage the solution should be injected *into a vein*, while the infusion of the sterile fluid which should be at blood temperature, should be carried out under some pressure in order to give an impetus to the insufficiently circulating blood.

As for the quantity of the fluid injected, if the infusion can be done soon after the hemorrhage, a smaller quantity of liquid may be used to see whether it is sufficient. In my

experiments in which the quantity of blood lost was known, four-fifths of this quantity was injected in the form of artificial substitute. If a longer period has elapsed, as a rule an immediate injection of larger quantities of sodium chloride solution will be necessary.<sup>1</sup>

Lastly, the quantity of fluid to be injected should be determined by the result itself of the infusion. This principle should, of course, be applied with reason and judgment.

#### SUMMARY

Several artificial blood substitutes have been compared to determine their action in acute dangerous hemorrhages. For that purpose fatal hemorrhages which were biologically equivalent were produced in different dogs, to discover whether the dog's life could be saved by the injection of blood substitutes into the blood stream.

In addition, a study was made of the influence of the infusion fluids on the blood, and of the hemorrhage and subsequent infusion of substitutes on the urine and sodium chloride excretion.

It was found that none of the infusion liquids gave better results than the sodium chloride solution.

A search and study of the medical literature on the subject of the substitution for blood of artificial fluids were carried out, and the facts revealed by the author's own experiments were complemented by those reported in the literature. The author also gives his opinion as to the results of infusion after hemorrhage.

The conclusion is reached that the injection into a vein of 0.9 per cent sodium chloride solution after an acute dangerous hemorrhage is preferable to the use of other artificial substitutes and to blood transfusion.

Directions are given as to the method of sodium chloride solution injection.

#### REFERENCES

- 1 BARCROFT, J. *Ergebn. d. Physiol.*, 1926, 25, 818-861.
- 2 BAYLISS, W. M. *Lancet*, 1922, Jan., p. 38.
- 3 Idem. *Lancet*, 1923, 204, 575-576.
- 4 Idem. *J. Am. M. Ass.*, 1922, 78, 1885-1887.
- 5 Idem. *J. Pharmacol. & Exper. Therap.*, 1920, 15, 29-74.

<sup>1</sup>In this connection I refer to the communication of W. F. MacFee and R. R. Baldridge, *Ann. Surg.*, 1930, 91, 329-341, who saw good results in conditions of shock (also as a consequence of great loss of blood) of the infusion into the circulation of for instance 3 to 5 liters of sodium chloride solution.

- 6 BUCK, A. Deutsche med. Wchnschr. 918, No. 4, 564
- 7 Idem. Deutsche med. Wchnschr. 918, No. 30, 247
- 8 BOWE, F. J. and VRAZIL, V. Rev. de med. 697, 7 835-905.
- 9 Idem. Rev. de med. 1899, 8 29-279.
- 10 Ibid. pp. 46-498.
- 11 B. ROBERT E. Progrès med. 1913, March, 43-432
- 12 Editorial. J. Am. M. Ass., 9 2, 78, 330
- 13 GIRAUD, J. and SALMON, P. Presse med. 990, Aug. 1913
- 14 GOLTZ, F. Arch. f. path. Anat., 864, 39 394-433.
- 15 HAMMERS, H. J. Researches made in the Physiological Laboratory of the Utrecht University 637 3d Series, No. 1, pp. 35-44 (Holl.)
- 16 HORTON, A. W. J. II. Are there artificialities with peculiar favorable action in hemorrhages. A comparative research on the action of several blood-substitutes in dangerous hemorrhages. Thesis de docit, Utrecht, 934, February (Holl.)
- 7 Idem. Generak. Bl., 934, 3rd Series, N. 5. (Holl.)
- 8 Idem. Nederl. Tijdschr. Geneesk. 934, No. 35 3937-393 (Holl.)
- 9 HOLLOVACHOVIC, L. Arch. f. Anal. Physiol. Physiol. Abstr. Supplement band, 1905, 32-243
- 10 MAC FEE W. F. and HALLERDOX, R. R. Ann. Surg. 930, 9 330-341.
- 11 NORMET, L. Presse med. 9 5, No. 3, 37
- 12 Idem. Paris med. 936, July 3
- 13 Idem. L'Action biologique des citrates métalliques. Brochure Pharmacie T. LERICHE, Paris
- 14 Idem. Bull. et mémo. Soc. mal. de cher. 1930, 35 243-253
- 15 Idem. Compt. rend. de l'Acad. d. Sc. 930, 23 354
- 16 Idem. Bull. Acad. de med. 19 3, 90 624
- 17 Idem. Bull. Acad. de med. 1924, 92 1906
- 18 Idem. Bull. Acad. de med., 1924, Dec. 3, 1470
- 19 Idem. Bull. Acad. de med. 930, Feb. 7 224 24
- 20 SCHERER, K. In. BIER, Handbuch d. norm. pathol. Physiol. 1926, 7: 16-229
- 21 SCHWARTZ, E. Med. Klin. 1930, 25 358
- 22 WEICHARDT W. and UNGER, H. Deutsche med. Wchnschr. 933, N. 30, 247
- 23 WYNO, S. J. J. Biol. Chem. 933, 55 431

## THE HYPERTONIC WET DRESSING

AN EXPERIMENTAL STUDY<sup>1</sup>

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THE exceptional therapeutic value of the wet dressing, and more particularly the hypertonic wet dressing in the care of infected wounds, is an accepted fact. The constant beneficial results seen clinically have established this principle as among the most valuable in modern medicine. Because of this general acceptance, the controversy as to the exact mode of action of the hypertonic wet dressing has long been forgotten.

It was Sir Almroth Wright's contention that a hypertonic solution in contact with a wound acted as a lymphagogue. In this way it drew out lymph which had spent its bacteriocidal energy and called forth fresh lymph together with phagocytic white cells. The outpouring of lymph was considered the all important factor because of the fact that the hypertonic solution disintegrated the white cells and inhibited much beneficial enzymic action.

Taylor, citing numerous experiments on the diffusion of salts and colloids, held that only water was drawn from the wound since the larger protein molecules diffused very slowly through the semipermeable membrane of the capillary wall. Taylor also felt that hypertonic solutions checked the migration of leucocytes to the surface and that those reaching the surface were quickly destroyed.

Present day knowledge holds to this latter belief. That is, only water diffuses out into the hypertonic dressing and salt passes back into the cells of the tissues. This process gradually slows down as an osmotic balance is established. There is a slight but constant diffusion of protein outward. This takes place at a constant rate regardless of the tonicity of the solution used. The hypertonic solution has little or no effect in sterilizing the wound (Landau). It is not known how important a factor the solution is in bringing phagocytic white cells to the infected tissues. Nor is it known how much of a detrimental effect the solution may have on the action of the white cells once they reach the site of infection.

A great deal has been written on the value of hypertonic wet dressings. This has been largely from a clinical and theoretical standpoint. Very little experimental work on this subject has been undertaken.

The data here recorded are the result of the writer's curiosity to know just how much fluid might be withdrawn from a given wound with a given hypertonic solution. It seemed desirable to ascertain whether the amount withdrawn was sufficient in any way to account for the beneficial results obtained clinically. It also seemed important to learn what effect different hypertonic solutions had upon the rate of diffusion of fluid from the wound. The writer has been unable to find any previous work on this particular phase in the treatment of infections. Because of this it was thought that the following report would be of interest.

After starting the work, numerous ramifications of the original problem were suggested. Some of these were studied and comments upon them are also given.

In all 152 experiments were run on wounds of varying size and age. For the sake of brevity, an individual tabulation of these determinations is omitted. They have been summarized in the discussion of the results and many are indicated in Figures 1, 2, and 3.

The animals used were rabbits. These were chosen because of the ease with which they could be handled during a series of experiments. The blood of a rabbit is slightly more hypertonic than that of man (11) but this slight difference should make little variation in the results obtained. There can be no valid reason for not comparing the findings in these experiments directly with similar situations and conditions in man.

The solutions tested included sodium chloride 85, 25, 5, 10 and 20 per cent, magnesium sulphate 16, 32, and 64 per cent, glucose 20 and 50 per cent. A mixture of half glycerine and half alcohol was also used.

<sup>1</sup>From the Department of Pathology, Indiana University School of Medicine, Indianapolis, aided by a grant from the Research Division.

## METHODS

The methods used were of necessity somewhat crude since the problem involved open wounds. The action of hypertonic solutions upon these wounds varied to a considerable degree. This was particularly true in the older wounds. In these there were marked differences in response to hypertonic solutions. Also in the older wounds varying amounts of fibrin were deposited upon the wound floor thus impeding a free fluid interchange. For these reasons the use of a granulating wound was largely discarded. Most of the experiments were done on fresh wounds having the abdominal muscle layer of the rabbit for a base. Only a very thin sheet of muscular fascia was allowed to remain covering the muscle. This allowed ample opportunity for a free osmosis between the capillaries of the muscle bed and the solution to be tested.

## DETERMINATION OF AMOUNT OF FLUID WITHDRAWN FROM THE WOUND

Using an etherized rabbit with shaved abdomen, a portion of skin and subcutaneous fat was removed. Much of the deep fascia was also excised, only the muscle fascia itself being left to cover the abdominal muscles. Little trouble was encountered from bleeding vessels but when this did occur the vessels were carefully ligated. Dimensions of the wound were taken and its area calculated. The wound areas varied in the different animals from 0.5 to 2.7 square inches. So as to have a standard of comparison the results obtained from the different trials were corrected so as to show the fluid change for one square inch of bare wound surface.

After the preparation of the wound a portion of a rubber glove was fastened to the surrounding skin margins by means of rubber cement. This proved quite satisfactory and this combination often would remain water tight for 3 to 5 days. Into the portion of rubber glove was then put exactly 5 cubic centimeters of the hypertonic solution to be tested. A gauze fluff was laid over the abdomen and held in place by means of a small jacket. This kept the fluid in contact with the wound and the movement of the rabbit promoted a certain amount of fluid circulation.

After varying time periods (1 to 24 hours) the fluid was drained from the glove and carefully measured. Again 5 cubic centimeters of the same or another hypertonic solution was introduced and the processes repeated. Often the first run was discarded because of fluid loss from moistening the entire area or because of coagling of blood. In so far as possible the experiments were run in succession so that a more accurate comparison might be made of various solutions on the same wound.

The fluid removed from the rubber glove was analyzed to determine the amount of salt present and from that the percentage of salt of this fluid was readily calculated. The methods used in determining the amount of the solute were as follows (5) sodium chloride by Volhard Arnold's method for chlorides, magnesium sulphate by Folin's method for sulphates, and glucose determination by Benedict's quantitative method. In the tests for sodium chloride and magnesium sulphate, protein was first removed from the samples by precipitation with tungstic acid, and determinations were then made on the protein-free filtrate. A protein estimation by Purdy's quantitative method for albumin was also done on many of the samples.

## DETERMINATION OF HYPERTONICITY OF WET GAUZE DRESSING

In this series of experiments it was desired to find out what hypertonicity was present in the gauze next to the wound tissues as compared to the gauze on the outer portions of a wet dressing. Layers of gauze (40-44 mesh) were applied to the same type of abdominal wound previously described. The dressing was saturated with the hypertonic solution to be tested. After varying periods of time (1 to 20 hours) the dressing was removed and the different layers tested for their salt concentration. This was determined by dissolving the salt from the layers of gauze into a known quantity of water and then analyzing this for its salt content.

## RESULTS

*Amount of fluid removed from wound by hypertonic solution.* As previously stated, the tests were corrected so as to give the amount

of fluid given up by a wound 1 inch square in contact with 5 cubic centimeters of hypertonic solution. The solution was held in contact with the wound by means of rubber tissue.

It was found that all the hypertonic solutions used caused approximately the same amount of fluid diffusion from the wound. The amount of this diffusing fluid was 1.2 to 1.5 cubic centimeters per hour for the square inch of wound surface. This constancy was remarkable when the wide range of hypertonic solutions used was considered. These varied from 2.5 per cent sodium chloride with a hypertonicity of 3 (as compared with physiological saline) to 20 per cent sodium chloride with a hypertonicity of over 23. There was no noteworthy difference when magnesium sulphate or glucose solutions were substituted for the salt.

Fluid continued to pour out into the enclosed rubber container until it reached a hypertonicity of approximately  $1\frac{1}{2}$  (1.3 per cent for sodium chloride). At this point the fluid started to reabsorb and continued at a rather rapid rate. In Figure 1 these features are shown quite well diagrammatically for 5 and 10 per cent salt solutions. The curves resulting from other hypertonic solutions have been omitted from this graph for clarity. Their upward slope, however, is identical with those illustrated.

There seems to be but one explanation for the fact that approximately the same amount of water is withdrawn from the wound, regardless of the hypertonicity or the agent. In removing such relatively large amounts of fluid the capillaries must of necessity be the source of supply, osmosis taking place through their walls. Solutions having a hypertonicity of 3 can withdraw from the capillary bed of the wound practically the same amount of water as those of much greater hypertonicity. Therefore, within the range of solutions tested, the water diffusing outward must depend upon the volume of blood brought to the wound. Also, this volume was not appreciably increased by the various hypertonic solutions used. From this the conclusion can be drawn that in any wound the amount of fluid removed by a hypertonic solution is directly

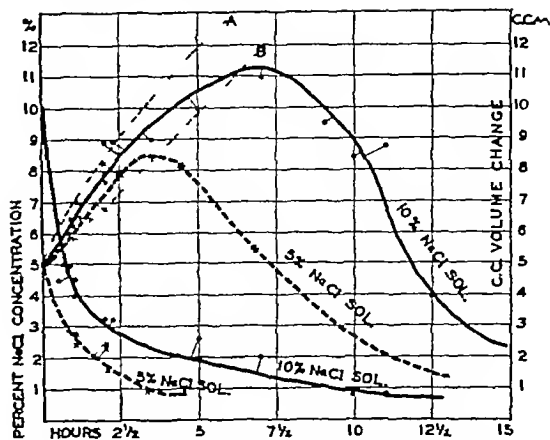


Fig 1 Showing the changes in volume and concentration of 5 cubic centimeters of 5 and 10 per cent sodium chloride held in contact with a square inch of wound surface. Curves of other solutions have been omitted. However, all tested concentrations of magnesium sulphate, sodium chloride, and glucose showed the same general rate of volume increase and their increase curves fell between the two dotted lines A and B.

proportional to the vascularity of that wound and bears little or no relation to the type or strength of solution used. This, of course, neglects the initial small amount of water which diffuses from the edematous tissues.

*Solute diffusion into wound tissues.* It was surprising to learn how rapidly a solution held in contact with a wound lost its hypertonicity. Part of this was of course due to a dilution by the outpouring water. However, a large factor was the diffusion of the salt into the wound. Thus 5 cubic centimeters of a 10 per cent sodium chloride solution in contact with a square inch of wound surface becomes 6.5 cubic centimeters of a 4.2 per cent solution at the end of an hour. In other words, 43 per cent of the original salt diffused into the wound tissues during this first hour. With weaker solutions this loss to the tissues was somewhat less. The same rapid loss of solute by diffusion was found with 20 per cent glucose solution.

It is well known that magnesium sulphate solutions diffuse but slowly into the tissue cells. Because of this they have for some time been advised for use in hypertonic wet dressings. It might then be expected that in our experiments the diffusion loss of magnesium sulphate solution was less than with sodium



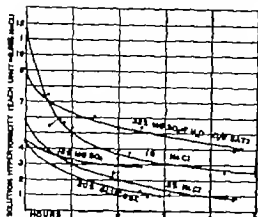


Fig. 1. Illustrating the rapidity of loss in concentration of various hypertonic solutions. It will be noted that the magnesium sulphate solutions maintained their concentrations much better than the other solutions indicated.

chloride or glucose. This was true but nevertheless the loss by diffusion of magnesium sulphate was quite appreciable. When 5 cubic centimeters of a 32 per cent solution (half saturated) was in contact with an inch square wound for 1 hour it became 6.2 cubic centimeters of a 22 per cent solution. This represents a loss by diffusion into the wound of 14 per cent in 1 hour.

The losses in hypertonicity of the various solutions in contact with the wound are shown graphically in Figures 1 and 2. The loss by diffusion is shown in Figure 3. Here it is clearly seen that the loss by diffusion is far less for magnesium sulphate solutions than for others which were tested.

**Effects of extremely hypertonic solutions.** Several extremely hypertonic solutions were tested upon the wounds. These included 50 per cent sodium chloride, 64 per cent magnesium sulphate (saturated solution at room temperature), 50 per cent dextrose and half alcohol and half glycerine. All these solutions caused a maximum amount of water to flow from the wound. This, however, only averaged approximately 10 per cent more than the milder hypertonic solutions and was always blood tinged showing that there had been actual damage to the capillaries. The wound tissues exposed to these very hypertonic solutions were found to be uniformly very edematous. The looser connective tissue assumed

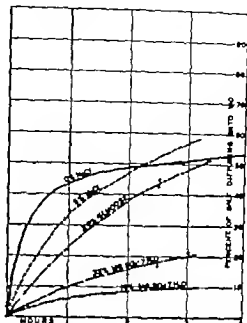


Fig. 2. Percent of the anions salts diffusing into the wound tissues. The relatively smaller loss by diffusion of magnesium sulphate is indicated.

quite a gelatinous quality. Much hemorrhage was found beneath the fascial membranes. This gave the wound a dirty brown necrotic appearance. Microscopic sections of the wound tissues demonstrated these same destructive changes.

In the light of this finding, it certainly seems inadvisable to use the extreme hypertonic solution advocated by some (1, 8). This is especially so since they draw but little additional fluid from the wound.

**Diffusible protein.** The amount of protein diffusing out into the hypertonic solution was quite constant as estimated by the Purdy quantitative test for albumin. It was proportional to the elapsed time and seemed to have little to do with the hypertonicity or type of solution used. Exceptions to this were in the older wounds and, when extremely hypertonic solutions were used, gross blood appeared in the fluid to be tested. In both instances the amount of protein was quite variable and usually high.

**White blood cells.** It would, of course, be desirable to determine the number of phago-

cytes drawn forth by the various hypertonic solutions. Attempts were made to do this but were abandoned because of the inaccuracies of such a procedure. The white cells in the very hypertonic solutions were largely destroyed and their remnants clumped together in plaque like masses. Those observed in solutions of lower hypertonicity were destroyed to a lesser degree, but counting chamber methods still gave results too variable to report.

*Gauze dressing analysis.* An analysis of the layers of a gauze dressing to determine the hypertonicity of these different layers was interesting. This was done with solutions of 5 and 10 per cent sodium chloride, 32 and 64 per cent magnesium sulphate. It was found that the innermost layers of gauze (those next the wound) were markedly decreased in their hypertonicity as compared with the outer layers. Thus when both 5 and 10 per cent sodium chloride solutions were used to saturate the dressing, the first two thicknesses of gauze next the wound had a 11 to 2 per cent concentration after 1 hour. This would indicate that it is only this hypertonicity (11 to 2 per cent sodium chloride) which is effective in drawing water from the wound.

When magnesium sulphate in the solutions previously indicated were used, slightly higher values were obtained. With the saturated solution (64 per cent), the innermost two layers were found to contain a 14 per cent solution. With the half saturated solution these same layers contained an 8 per cent solution. It should be stated that an isotonic solution of magnesium sulphate is 3.52 per cent ( $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ ).

Another finding of clinical interest was the fact that when there was the least bit of bloody ooze from the wound, the two inner gauze layers were quite isotonic. Therefore the hypertonic solution would be absolutely ineffective in extracting fluid by osmosis. As there is always a bloody ooze from a recently incised abscess, it should be remembered that action of a hypertonic wet dressing to such a lesion is nil as regards its water extracting power.

#### EVALUATION

It has been shown that the amount of fluid capable of being withdrawn by a hypertonic

solution from 1 square inch of wound surface is 12 to 15 cubic centimeters per hour. This amount varies between these figures regardless of the hypertonicity or nature of the solution. In general the more concentrated solutions gave the higher figure but to all practical purposes they were identical. This at least held true for solutions with a hypertonicity between 3 and 23 (2.5 and 20 per cent sodium chloride).

The values given are maximal for the animals used. They represent figures for new wounds with vascular muscle bases. In older wounds which had started to granulate and the surfaces of which were partly covered by fibrin, the values varied to a considerable extent in different animals and were found to be lower.

It is pointed out that the fluid withdrawn by a hypertonic solution is water and not serum similar to that seen in burns (7,9). It contains only the amount of protein material which would normally diffuse from the wound. There is no increment of this caused by the hypertonic solutions. The value of this withdrawal of water from the wound seems to the writer to be a debatable question. For, after the initial dehydration of the surface tissues, the continued outpouring comes from the blood vessels themselves and is directly dependent on the vascularity of the area. Also in all wounds except those exposed to the lower concentrations of magnesium sulphate, the wound tissues continued to absorb enough salt to maintain in themselves quite an edematous state.

It has been stated that an increased flow of water to the surface brings an increased number of phagocytes (4). This seems probable but the amount of this increase is still unknown. Also the literature relating to the specific ion action (2) and enzymic action resulting from the use of various solutions is unconvincing.

It should be further pointed out in the light of the foregoing experiments on wet dressings that an effective hypertonic solution reaches only the superficial tissue. That the deeper tissues containing the active infection can not possibly be reached by the salt solution is quite evident.

Wherein, then, lies the great value of the hypertonic wet dressing? It is thought that by far the chief benefit derived from this type of dressing is its poulticing action. This keeps the skin soft and pliable. It prevents crusting of the wound and allows drainage to continue. Above all it soon becomes warmed by the body and this markedly increases the flow of capillary blood (3) thus improving the defense mechanism against infection.

Bearing out this contention is the fact that isotonic saline and even hypotonic solutions (1:5000 mercuric chloride) have been seen to give the same beneficial effects noted in hypertonic solutions.

It is not the purpose of this paper to discredit the use of hypertonic solutions but merely to point out that the withdrawal of fluid which they effect from the infected wound is of only minor importance. Their principal benefit must be from a poulticing action. It would seem that the most beneficial results might be expected from a mildly hypertonic magnesium sulphate solution (16 per cent  $MgSO_4 \cdot 7H_2O$ )

## REFERENCES

- BRIDLEY, F. A. Problems involved in treating compound fractures. *Surg. Gynec. & Obst.*, 434-79, 1-4.
1. GASA, W. Von. Effect of hypertonic salt solution on granulation tissue. *Zentralbl. f. Chir.*, 472, 50, 191.
2. GOLDSCHMIDT, S. and LACART, A. B. The effect of local temperature upon the peripheral circulation. *Am. J. Physiol.*, 27, 73, 146.
3. GREENE, W. R. Some effects of solutions on open wounds and their practical application. *Cincinnati J. Med.*, 93, 3, 300.
4. HAYK, P. B. and BERGEN, O. Practical Physiological Chemistry 9th ed. Philadelphia: Blakeman, Son Co. 1936.
5. LAURMAN, H. Experimental research on hypertonic saline in the treatment of wounds. *Arch. f. Klin. Chir.*, 93, 1, 6.
6. LAYTON, E. M. Capillary pressure and capillary permeability. *Physiol. Rev.*, 23, 14, 404.
7. ROBERTS, J. E. H. and S. TRANT, R. S. S. The salt pack treatment of infected gunshot wounds. *Brit. M. J.*, 9, 4, 25.
8. TAYLOR, K. Mechanism of saline dressings. *Brit. M. J.*, 9, 6, 3.
9. UNTERHILL, F. P. KAPRANOFF, R., and FOX, M. E. Studies on the mechanism of water exchange in the animal organism. *Am. J. Physiol.*, 1930, 93, 313.
10. WAGGONER, G. and COOPER, R. P. A Handbook of Experimental Pathology. Springfield: Charles C. Thomas, 1931.
- WHEAT, A. E. Monoculization on the treatment of infected wounds by physiological methods. *Brit. M. J.*, 19, 4, 703.

# CLINICAL SURGERY

FROM THE NEW YORK HOSPITAL AND CORVELL MEDICAL COLLEGE

## COLOSTOMY OF THE TRANSVERSE COLON

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**I**N A recent publication entitled "Origins and Evolution of Colostomy," Dinnick, of London, reviews the history of colostomy. He refers to the biblical book of Judges, in which we find an account of the foul murder of Eglon, King of Moab, by Ehud. Ehud stabbed him in the belly with his dagger and "the dirt came out." This may be the earliest written report of opening the colon, but hardly can it be considered a record of a therapeutic colostomy. The first deliberate colostomy is ascribed to Littre, who, in 1710, devised this operation for the treatment of imperforate anus. That he actually performed such a surgical procedure we have no evidence. However, Pillore, DuBois, Duret, and Desault, in the eighteenth century, opened the sigmoid colon in treating imperforate anus. Fine is said to have performed the first colostomy of the transverse colon quite by accident in an attempt to open the small intestine through a midline incision just above the umbilicus. The nineteenth century witnessed an increase in colostomies which then were used also in the treatment of intestinal obstruction due to malignancy. In 1853, Hawkins reports that 44 such operations had been recorded in the literature and that the procedure was attended by a 50 per cent mortality due to the fact that it was invariably followed by peritonitis. The work of Pasteur and Lister, which so revolutionized surgery, increased the safety of this procedure.

Inguinal colostomy originally was the operation of choice, but later was supplanted by lumbar colostomy. The pioneers in this field of surgery encountered difficulty in closing the artificial anus which they had made. Prior to the nineteenth century it was believed that the section of bowel which had been used for the colostomy must be resected. Obviously this entailed an intestinal anastomosis, a procedure of such magnitude in those days that it carried with it a high mortality. This difficulty was obviated when it was found that a small opening in the bowel suf-

ficed, for this was simple to close. The repaired bowel, then, could be returned to the abdomen through the defect in its wall with or without entering the peritoneal cavity.

A review of the last 25 years shows that surgeons have directed their efforts mainly toward perfecting the permanent colostomy. With this aim in view, they have devised several ingenious methods of procuring control of the artificial anus. The horror of patients, ignorant of colostomy, when they are told that such a procedure is imperative in the treatment of their disease, is minimized if they can be promised some means of control. It has been the prevailing opinion that the best results are obtained by placing the colostomy near the site of the obstruction, a logical procedure when permanent colostomy is concerned. It is the object of this discussion to point

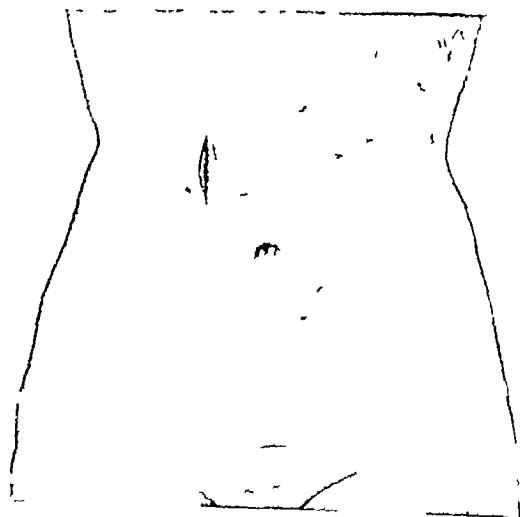


Fig 1 The transverse colon is approached through a vertical incision, 6 centimeters or more in length, over the midportion of the right rectus muscle just above the umbilicus.

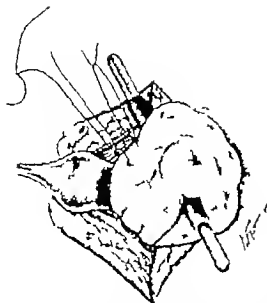


Fig. 4 With interrupted sutures of monofilament silk the pen-tosoma is secured to the bowel where it emerges from the abdominal cavity. When these sutures are tied the same silk is used to bring the exterior sheath together. The dotted line indicates the incision for the colostomy tube.

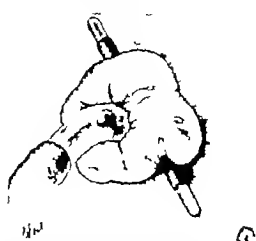


Fig. 5 The large caliber glass tube is anchored with penetrating suture. The glass rod is shown in place under the exteriorized loop of intestine.

ut the advantages of establishing a temporary colostomy at some distance from the lesion.

The description of transverse colostomy is given, without claim to originality, with the idea of promoting this operation as an important step in the treatment of lesions of the descending colon, the sigmoid, and the rectum, a step which simplifies the eradication of the lesions. The rationale of this operation, the technique of the surgical procedure, the care of the completed colostomy, and its closure will be discussed in turn.

A temporary colostomy is designed to decompress the large bowel partially or wholly obstructed by a lesion below the splenic flexure. In preparation for the removal of the lesion. When an obstruction has persisted for some time the wall of the bowel proximal to the obstruction becomes edematous and sometimes hypertrophic. The anastomosis of a collapsed segment of bowel below the obstruction (an edematous hypertrophic portion above it) is a procedure which is rarely satisfactory. If the bowel above the lesion is decompressed and kept evacuated, it is given an opportunity to return to a normal state before the removal of the lesion is attempted. The anas-

tomosis, then, can be carried out under more favorable conditions. A preliminary colostomy is equally important as a means of improving the patient's general condition, in preparation for the formidable procedure of resection which is to follow. A malignant tumor of the large bowel is rarely a rapidly growing lesion and the time consumed in building up the patient's resistance is well spent.

There are two arguments in favor of transverse colostomy. First, there is no portion of the large bowel, with exception of the rectosigmoid, which is as freely movable as are the hepatic flexure and the first part of the transverse colon. Long mesenteric attachments facilitate the delivery into a right rectus wound of this section of bowel. The intestine through which the fecal stream passes before reaching this region frees the contents of most of the digestive elements. Such make the care of an ileostomy or rectostomy so difficult. Second a transverse colostomy high on the right side of the abdomen, is far removed from the operative field in the resection of the lesion and does not endanger the asepsis of this major operation.

Transverse colostomy is not a major procedure. It can be carried out under local anesthesia with little danger to the patient immediately though he may be in poor condition because of long standing obstruction or of complications of intestinal pathology necessitating surgical intervention. Even though an exploration following the colostomy reveals an inoperable growth warranting a permanent artificial anus, nothing has been lost.

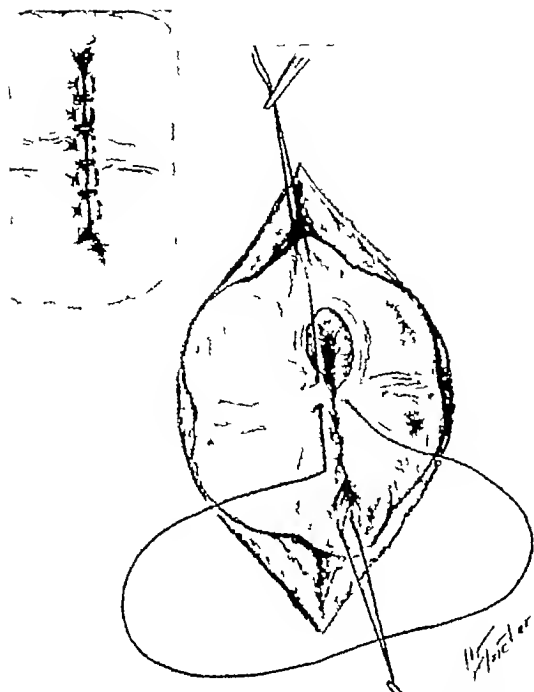


Fig 4 The incision into the colon is closed transversely with respect to the axis of the bowel. Silk traction sutures are placed in the intestinal wall laterally, with traction exerted upon these sutures, a continuous catgut suture is introduced through the entire wall to unite the serosa on either side and thus to invert the mucosa.

by the preliminary emergency colostomy of the transverse colon which is closed without difficulty. If the tumor can be resected, this type of colostomy offers the greatest protection against contamination of the clean wound. In an analysis of the deaths in any series of cases treated for malignant disease of the colon below the splenic flexure, it will be seen that infection is the most serious complication.

#### THE OPERATION

The transverse colon is approached through a vertical incision, 6 centimeters or more in length, over the midportion of the right rectus muscle just above the umbilicus (Fig 1). After the skin and subcutaneous tissues have been incised, the anterior rectus fascia is divided, the muscle fibers on either side of the incision are freed and the muscle split with a blunt instrument to the full extent of the skin incision. The posterior rectus sheath, which is now exposed, is grasped with a forceps and incised with the peritoneum lying below it. A hemostat is placed on each side of the

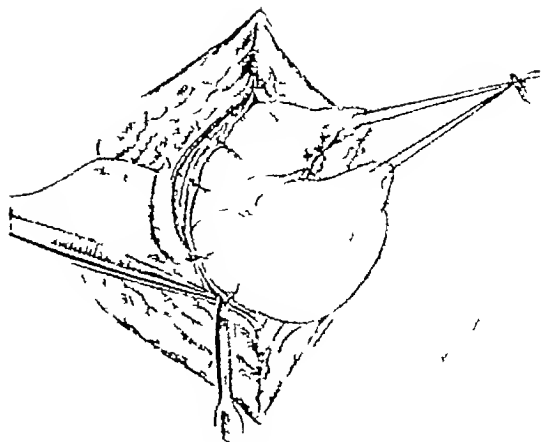


Fig 5 After closure of the bowel, the fascia is separated from the point of union with the peritoneum by dividing the silk sutures as placed in Figure 3.

opening in the peritoneum, which is extended the whole length of the incision. The colon usually lies directly in the field and is now delivered through the abdominal wound and inspected. If the omentum covering the bowel is freed at its attachment to the extramesenteric border, it may be returned to the abdominal cavity. A rent is made in the transverse mesocolon under the loop and a glass rod is inserted through the opening to aid in maintaining the bowel on the outside of the abdomen.

The closure of the wound is designed (1) to anchor the intestine, (2) to prevent the peritoneum from tearing, (3) to isolate the rectus muscle, and (4) to avoid herniation of the bowel. With interrupted sutures of medium silk the peritoneum is secured to the bowel where it emerges from the abdominal cavity (Fig 2). Sutures are placed above and below the glass rod and at either end of the peritoneal incision to prevent it from tearing. When this level of the wound has been closed and the sutures tied, the same silk is used to bring the anterior sheath together. In this way the muscle is isolated on either side of the wound where it cannot attach itself to the intestine, this facilitates the eventual closure of the colostomy. Skin sutures are introduced at the extremities of the wound so that the skin is approximated snugly to the bowel without tension. If the abdominal wall is thick, an attempt is made to sew the fascia to the skin, to prevent the bowel from pocketing under it in the subcutaneous fat. If this procedure is not carried out in stout patients, the bowel may retract below the



Fig. 6

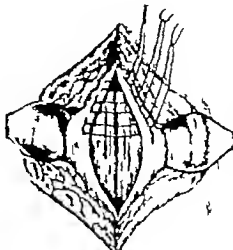


Fig. 7



Fig. 8

Fig. 6 The closure of the peritoneal layer is accomplished by the application of continuous chromic catgut suture.

surface and close spontaneously. The obese patient with a thick abdominal wall is best guarded against abscess formation by allowing 36 to 48 hours to elapse before opening the colostomy.

At the completion of the operation vaseline gauze is applied to the skin where it joins the bowel wall and the bowel is veraled with the same material. The final dressing is a soft gauze pad held in place loosely so as not to interfere with the passage of gas and fluid fecal material through the externalized loop. This dressing is not disturbed until the bowel is opened.

*Decompressing the bowel at the time of operation.* In patients who have been distended for a long time or in whom the distention is causing marked discomfort, it may be necessary to decompress the bowel at the time of operation. With all steps of the procedure completed, including the application of the vaseline gauze over the loop of colon, a small area is exposed and two pursestring sutures are placed so as to encircle the point selected for the introduction of the needle. With a bichloride sponge protecting the bowel, a lumbar puncture needle (N. 20) is inserted into the lumen, through which the gas escapes. When the tension has been relieved, the pursestring sutures are drawn tight and secured around the needle as it is withdrawn. The site of the puncture is

Fig. 7 The external rectal sheath is overlapped and sutured with interrupted chromic sutures.

Fig. 8 The external rectal sheath closed.

cleansed with alcohol and a bichloride sponge is held in place over it by the vaseline gauze. If the bowel is distended with fluid feces as well as gas, it may be considered wise immediately to institute continuous drainage for this purpose either a catheter or a glass tube may be inserted into the loop and secured with sutures. Care must be exercised not to contaminate the fresh wound with fecal material. Pursestring sutures are placed as described for the needle puncture. The bowel, protected with bichloride sponges, is held with forceps and incised with a scalpel the catheter is introduced through the opening. The pursestring sutures are secured about the catheter and the bowel wall drawn about it by a series of medium silk mattress sutures after the method of Witzel for a distance of 3 centimeters from the bowel wall opening. A small rubber tube attached to the end of the catheter leads fecal material into a bottle by the bedside. If a glass tube is used instead of the catheter it is introduced and anchored in the same way. The tube should be L-shaped and small, for it is difficult to avoid contamination of the wound if too large a tube is introduced at this time. The immediate establishment of drainage is never the method of choice, but serves when relief from distention is imperative.

*Opening of the colostomy* It is much safer to delay the opening of the colostomy until the second or fourth postoperative day, for the danger of contamination and infection of the wound is diminished by waiting. If the patient is not suffering acute symptoms of obstruction and the colostomy is a step in preparation for the major operation, this problem need not be faced, for the fecal stream follows its natural course. When the lesion in the lower bowel is causing grave signs of obstruction and the restriction of food and fluids by mouth fails to relieve the discomfort of the patient, the bowel must be opened earlier.

The incision into the bowel, made with a scalpel or cautery, is longitudinal and carried through the tenia opposite the mesenteric attachment. It should be only of sufficient length to admit the tube, which in this case is of larger caliber than the one described for immediate decompression of the bowel. This larger tube (2 centimeters in diameter) does not so easily become clogged by semifluid feces, and a catheter may be introduced into the bowel through it to wash out solid fecal material. The tube is anchored as described above (Fig 3).

*The care of the colostomy before the tube is removed* The tube which is inserted into the bowel when the colostomy is opened usually stays in place until the sixth or seventh postoperative day. Before it is removed, the care of the colostomy is not difficult, for the fecal material drains through it directly into a bottle by the bedside. The consistency of the fecal stream can be controlled by diet and by the administration of mineral oil or other mild laxatives. If the intestinal contents are not liquid, the tube may become clogged, but irrigation will relieve any obstruction of this kind.

*Removal of the glass rod* The glass rod, introduced through the mesentery under the loop of bowel delivered into the wound, is usually removed before the drainage tube is withdrawn. It may be left in place (a) if the intestinal loop tends to retract, as it may if a short mesentery keeps it under tension, or (b) to prevent any fecal material from passing into the bowel below the colostomy.

*The care of the colostomy after removal of the tube* After the drainage tube has been removed, there is no way of carrying the fecal stream beyond the confines of the dressing. Although this is not as serious a matter in transverse colostomy as it is in ileostomy or cecostomy, the skin may become irritated by contact with feces. This excoriation may be prevented by the application of aluminum paste (aluminum metal 50 parts, zinc oxide 450 parts), which adheres closely to the skin. The coat of paste must be renewed every 2 or 3

days. An absorbent dressing is kept over the colostomy until it is completely healed.

*The care of the bowel distal to the colostomy* When the lumen of the bowel has been completely occluded by a lesion, the segment of intestine between the obstruction and the colostomy requires particular care. Daily irrigations with saline will cleanse it of fecal material and debris, instillations of a saturated solution of magnesium sulphate will reduce the edema. Provided these treatments are given with care not to cause hemorrhage, they are the best means of restoring the bowel to its normal state. If the obstruction at the site of the lesion has not been complete, through and through irrigations with saline followed by instillations of oil will keep the gut clean and will tend to allay some of the congestion. This procedure should be carried out once a day.

*The care of the colostomy by the patient* As soon as the patient is ambulatory, he must be taught the means of avoiding unnecessary discomfort and inconvenience from his colostomy. He learns to regulate his diet so that his stools are not too soft or liquid. He becomes familiar with the sensations which warn him of impending movements, this enables him to adjust his life so that the colostomy causes him the minimum of inconvenience. A colostomy bag may add to his feeling of security at first, but it is frequently discarded as soon as the patient discovers that a degree of constipation enables him to reduce the evacuations of his bowels to one or two a day. A dressing of absorbent material guards against soiling.

*Closure of the colostomy* Closure of the colostomy may be accomplished in one of two ways, i.e., extraperitoneally or intraperitoneally. The exteriorized bowel segment must be liberated before its closure can be undertaken. The initial steps are the same in both procedures. An incision is made in the skin following the outline of the old scar, but leaving a narrow margin of skin attached to the bowel. The subcutaneous tissues are bluntly dissected off of the bowel down to its junction with the external rectus sheath. The sheath is divided, again leaving a margin around the entire loop of colon. The muscle which is now exposed, is reflected away from the junction of the external sheath and the peritoneum, the line of silk sutures which united these surfaces at operation will act as a guide to this junction and having served this purpose they may be removed (Fig 5). The margins of skin and external rectus sheath which were left attached to it may now be stripped off of the bowel by sharp dissection. Excepting for its attachment to the internal sheath



and peritoneum, at the base of the wound, the intestine now lies free and the closure of the opening in the bowel may be carried out as follows. The incision into the colon, which, as will be recalled, was made in a longitudinal direction, is closed transversely with respect to the long axis of the bowel, in order to prevent narrowing of the lumen. Silk traction sutures are placed in the intestinal wall laterally; traction on these sutures will bring the sides of the opening together across the long axis of the bowel. In this position a continuous catgut suture is introduced through the entire wall to unite the serosa on either side and thus to invert the mucosa. A series of interrupted mattress sutures of silk are now placed in the serosa and these in turn are reinforced by single interrupted sutures of the same material placed between the mattress sutures (Fig. 4). At this stage in the procedure the operation is interrupted while the operative field is cleaned, the wound re-draped with clean towels and the entire surgical set up replaced by a new one. The closed bowel is now invaginated through the defect in the abdominal wall, and over it the peritoneum is approximated with a continuous suture of chromic catgut (Fig. 6). The muscle is freed, so that it may resume its normal position across the center of the wound. The external rectus sheath is overlapped and sutured with interrupted stitches of chromic catgut (Figs. 7 and 8). One stay suture holds the skin, subcutaneous tissues, and fascia together; a rubber tissue drain is inserted down to the fascia and the skin is approximated with interrupted sutures of fine silk.

When the wound has been opened down to the peritoneum as described and the bowel, thereby is not sufficiently liberated to permit its closure, or if there be herniation of omentum or any of the abdominal contents between the bowel wall and the peritoneum, as may sometimes be the case, then the peritoneum must be opened. An incision is made close to the intestinal wall and carried around the entire loop. This makes it possible to draw the bowel further out through the wound. With the peritoneal cavity carefully protected with gauze pads, the closure of the orifice in the bowel is undertaken as previously described. If adhesions are present between the colon and the peritoneum, these are freed and the bowel is re-

turned to the abdominal cavity. The peritoneum is closed with a continuous suture of chromic catgut and the subsequent steps in closing are as described.

Intraperitoneal closure is never the method of choice but although the peritoneal cavity must be considered grossly infected in an intraperitoneal closure, localized abscess formation or peritonitis rarely follows this procedure—a fact which gives evidence of the establishment of a local immunity.

*Postoperative care after closure of the colostomy.* Nothing is given the patient by mouth for a period of 24 hours after closing the colostomy and for an additional 48 hours the intake is restricted to clear fluids. This routine has been adopted in an effort to reduce peristalsis to a minimum during the first postoperative days. If the bowel can be kept quiet for 48 to 72 hours, there is little danger of intestinal obstruction or of a fecal fistula developing at the site of the closure. Seventy-two hours after operation the patient is given a soft diet and mineral oil as a laxative.

The drain is removed at the end of 48 hours. If there is an unusual amount of reaction around the wound at this time warm moist saline dressings are applied.

The patient is allowed up on the eleventh post operative day.

#### SUMMARY

1. A brief history of colostomy is given, including reference to the recent developments.
2. Transverse colostomy is recommended as a step in the preparation for the removal of a lesion of the lower bowel or rectum.
3. The rationale of this operation, the technique of the surgical procedure, the care of the completed colostomy and its closure are discussed.

#### BIBLIOGRAPHY

- DEBAILLÉ, P. J. *J. de chir. de Doualt*, 791, 4, 115.  
 DORVILLY, T. *Origine and evolution of colostomy*.  
*Bull. J. Surg.* 1915, 21, 4.  
 3. DEBAILLÉ, P. *Rec. périodique Soc. méd. de Par.* 791, 1, 13.  
 4. DUBREUIL, C. *Rec. périodique Soc. méd. de Par.* 791, 4, 45.  
 5. FROST, A. *Ann. Soc. de Montpellier*, 797, 6, 34.  
 6. H. WATSON, C. *Med. Chir. T.* 812, 11, 85.  
 7. LITTRE, J. *Hum. Acad. d. sc.* 710, p. 17.  
 8. PILLON, H. *Gaz. de hôp. de Par.* 790, 10, 11.

KRAUROSIS VULVÆ (LEUCOPLACIA) AND SCLERODERMA  
CIRCUMSCRIPTAA COMPARATIVE HISTOLOGICAL STUDY<sup>1</sup>

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IN July, 1932, a patient, with the diagnosis of kraurosis vulvæ, was referred to the Department of Dermatology from the Gynecological Dispensary for advice because of the severe itching associated with the disorder. During the examination, it was discovered that she had lesions also on her body resembling those of a variety of circumscribed scleroderma which has been described as white spot disease. This association stimulated us to make a comparative histological study of these two affections including, also, several cases of the morphea type of scleroderma. The patient referred to will be considered in full, and a brief summary of a second case of white spot disease, without vulvar lesions, will be included. The histological findings in these cases will be compared with those of kraurosis vulvæ, the material for which was obtained mainly from the Gynecological Laboratory through the courtesy of Dr. Cullen.

## REVIEW OF LITERATURE

*A kraurosis vulvæ* This name was introduced by Breisky in 1885 to describe a condition of the female genitalia characterized by a peculiar atrophic shrinking of the skin affecting the vestibule, small labia, inner surfaces of the large labia up to the posterior commissure and bordering part of the perineum. The frenulum and prepuce disappear and the small labia are represented only by a white line. The affected skin is white and dry where retraction is most pronounced, while in other areas it is shiny, dry, pale, reddish gray with whitish spots and dilated capillaries. The condition causes a marked vestibular stenosis interfering with childbirth and coitus.

Since kraurosis in the restricted Breisky sense is usually associated with a spotty or diffuse whitish appearance resembling leucoplacia, a great deal of confusion has arisen as to the relationship of these two conditions. Some writers believe that leucoplacia and kraurosis are two distinct diseases, while others consider them different manifestations of the same pathological process. In the former group, Berkeley and Bonney take the most extreme view, their description of the two affections as abstracted by Graves and Smith, is as follows:

*Leucoplacic vulvitis* is a chronic inflammatory condition of unknown origin characterized in its early stages by marked hyperemia and cellular activity, and in its later phases by marked epithelial hypertrophy, and a thickened, sclerosed and retracted condition of the subepithelial tissue. The whole of the vulva may be implicated with the exception of the vestibule and orifice of the urethra, which are never affected. It may extend laterally to the folds of the thigh and posteriorly to the external perineum and the skin around the anus. There are four clinical stages:

First stage: reddening, swelling, excoriation, and dryness.  
Second stage: retraction with thickening, decrease in size of the greater and lesser lips, and change of color from red to white.

Third stage: cracks and ulcers with discharge and bleeding, tendency to carcinomatous change.

Fourth stage: complete involution, vulval surface smooth, shiny and white, disappearance of labia minora and clitoris from contraction of the subepithelial tissues, cessation of pruritus.

The symptoms are intense pruritus in the second and third stages and pain with acute sensitiveness in the third stage from the exposure of nerve endings in the cracks and ulcers. There are no symptoms in the fourth stage.

*Kraurosis vulvæ* consists of an atrophic condition of the vulva associated clinically with stenosis of the vaginal orifice and pathologically with certain changes in the dermis. It may involve all the surface of the vulva as far as the skin borders of the labia majora, and the skin of the perineum and anal region. Kraurosis vulvæ is divided into two stages:

First stage: the mucocutaneous surface, red and glistening, is dotted over with small patches varying in color from bright red to purple. The urethral orifice is in a caruncular condition.

Second stage: the mucocutaneous surface becomes yellow like that of a fatty liver. The surface ridges are obliterated. The vaginal orifice is greatly contracted, the labia minora and clitoris disappear, the mons veneris atrophies, the pubic hair breaks off or falls out. The condition is one simply of retraction and thinning. Pruritus is one of the rarest symptoms, the chief complaint being that of dyspareunia. In the first stage, the parts are sensitive, especially to the passage of urine.

Graves and Smith on the other hand, maintain that Berkeley and Bonney's leucoplacia corresponds to what clinicians generally, at least in America, call kraurosis or if they are more exact, kraurosis with leucoplacia, and that their kraurosis is clinically a marked or progressive genital atrophy. Graves and Smith believe that leucoplacia and kraurosis are phases of the same pathological process, and while they recognize the inadequacy of the term "kraurosis," since it characterizes only the shrinking stage of the process, they would let this term be the nickname rather

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of the whole disease, which, beginning with an irritative vulvitis, is signalized by pruritus, under goes superficial epidermal changes in the form of leucoplasia, and deeper dermal changes that result in shrinking and retraction.

These opinions will serve to illustrate the confusion existing with reference to these two processes and in the present communication, we will use the terms leucoplasia and kraurosis vulvæ more or less interchangeably.

The histological findings of different authors in kraurosis and leucoplasia have varied considerably. In one of Breisky's original cases studied by Professor Chiari, an involuntary process was found in the upper corium the substance of which was sclerotic and glassy. In some papillæ, but more specially in the deeper layers of the cutis, there was a small, round cell infiltration. The epidermis showed a hyperkeratosis with shortening of the rete pegs.

Berkeley and Bonney describe the histology of leucoplasia in several stages:

1. Swollen epithelium, increased vascularity and lymphocytic infiltration in the cutis.

2. Lymphocytes still conspicuous, plasma cells appear and there is an increased number of large, hyaline, fixed connective tissue cells normal to the part. The sustentacular elements become altered, the white fibers are decolagenized, and become more hyaline in appearance with a loss in many areas of the elastica producing a zone between the epithelium and deeper tissues. New lymph nodes appear containing areas showing cell division. There is marked hypertrophy of the epithelium.

3. Cellularity of cutis begins to give place to a fibrosis and many of the inflammatory cells disappear. There is a redeposit of collagen around the fibroglia fibers of the fixed connective cells, which in the preceding stage had been greatly increased in number. The previously rarefied tissue now becomes denser than normal, hypertrophy of epidermis persists, but a marked hyperkeratosis has developed. There is total absence of elastica.

Final stage. Complete sclerosis, very few cells remain. atrophy of epithelium.

The histology of kraurosis vulvæ according to these authors is quite unlike that of leucoplasia. In kraurosis, the subepithelial connective tissue exhibits marked patchy cellularity. In the clinically red areas there may be massive plasma cell proliferation, mixed with, or surrounded by lymphocytes and polymorphonuclear leucocytes. A striking feature is the intercalation of the leucocytes between the epithelial cells. The elastic tissue is present except in the masses of plasma cells. The epidermis is thinner than normal.

Jayle and Bender in writing on leucoplasia of the vulva, emphasize particularly the changes in the epidermis and believe that the thickening of the granular layer both in its cellular component as well as the number of granules in the cells is pathognomonic of the affection. They admit, however that this may fall in certain stages of the process, when a series of alterations irritative or degenerative occur. The *clivus* (?) layer may then atrophy and disappear. The dermis proper is markedly altered. The connective tissue is dense and fibillary, and there is a considerable leucocytic infiltration more marked in the upper zone. The infiltration is composed mostly of small mononuclear cells, abundant plasma cells, and a few polymorphonuclear and mast cells. The collagenous tissue is abundant but does not take the color by Van Gieson's stain as intensely as normal. The elastic tissue is augmented, thickened, and degenerated in the deeper layers. In the upper layers, it is fine and nodulating but not increased. They state that it is certain that leucoplasia and kraurosis vulvæ can co-exist but they had followed cases of the latter affection for years that did not develop leucoplasia. Later on, Jayle looked on kraurosis as the end stage of ordinary vulvar sclerosis. Its histology was characterized by alterations in the epidermis, which was usually atrophied, and a very dense sclerosis in the cutis which was rich in collagen and degenerated elastica.

Smaaz, who believes that kraurosis vulvæ is the end stage of leucoplasia found in the latter a high degree of acanthosis and hyperkeratosis, a loose connective tissue richly poor in elastica and rich in collagen, while in kraurosis there was atrophy of the epidermis associated with a firm connective tissue, almost free of collagen but rich in degenerated elastic tissue.

Gårdlund was struck by the edema and the peculiar elastic tissue changes (hyalination) which were present in the histological material from 3 of the 6 cases which he reported. In Case 1 some of the papillæ had a homogeneous, glassy, structureless appearance, while others presented an interstitial edema with a stretched reticular connective tissue. In Case 2, the papillæ were edematous with a homogeneous, hyaline or fibillary appearance while in Case 3 the entire subepithelial layer was markedly hyalinized. Interstitial edema was present only on the border. He does not believe that there is an increase in connective tissue, but due to the edema the bundles are not only swollen but may be ruptured. A cellular infiltration was present in the lower cutis below the changed elastic tissue. The elastic tis-

sue was absent in the upper edematous or hyalinized areas, while it seemed thicker than normal in the lower unaffected layers of the cutis

The author believes that the epidermal changes are relatively unimportant, and that the hyperkeratosis and thickening occasionally met with are due entirely to external irritation

In Peter's case the epidermis was raised up by an evadate containing leucocytes, fibrin, pigment, and amorphous masses. Connective tissue was structureless, and there was a round cell infiltration in the lower cutis with atrophy of elastica

Goerdes found in the corium a peculiar, glistering, glassy appearance of the connective tissue which had lost its fibrillar appearance. It was poor in vessels and cells, and elastic tissue was absent. There were collections of cells in the subcutaneous tissue. The epidermis was atrophic

Terruhn believes that there is an intimate relationship between leucoplacia (he calls it leucoderma and the most characteristic change is the loss of pigment) and kraurosis vulvæ but they are not always associated. In well advanced cases of kraurosis vulvæ, leucoplacia can always be found histologically. In the early stage of the disease, there is hyperplasia of the epidermis and, most important, disappearance of the pigment in the basal layer. This is accompanied by a marked edema in the cutis causing a pressure atrophy of the connective and elastic tissues. The former degenerates, appears homogeneous and swollen, but does not completely lose its structure and nuclei. This is followed by a regenerative stage manifested by a loss of the edema and a cellular reaction composed of capillary sprouts, connective tissue and plasma cells, lymphocytes, and a few polymorphonuclears. He interprets this as granulation, and not inflammatory, tissue. In the atrophic stage there is marked atrophy of the epidermis and the granulation tissue in the cutis has been replaced by a firm, fibrous connective tissue. All three stages may be found in the same section.

Graves and Smith, in the histological study of 18 cases, which showed the condition of kraurosis, found that the squamous epithelium was thinner than normal, the papillæ being short and thin or completely flattened out. The corium was very dense, elastic tissue was entirely absent, glands and hair follicles wanting, blood capillaries sparse, and throughout there was a greater or less round cell infiltration. In all of their specimens, however, areas were found which showed leucoplacia, i.e., a thickening and hyperkeratosis of the epidermis. They state that when leucoplacia is present, the corium is denser than normal but less

so than in kraurosis alone. Blood capillaries are infrequent, gland and hair follicles are sparse and atrophied, elastic tissue is decreased, and there is always a marked infiltration of round cells. In other words, the only essential difference between leucoplacia and kraurosis, is the greater activity in the former of the squamous epithelial layer.

Taussig prefers the name leucoplacic vulvitis reserving the term kraurosis for those cases in which there is a complete symmetrical atrophy of the labia and prepuce with flattening of the folds. He feels that it is the leucoplacia and not the shriveling of the skin which is of the greatest importance. He studied microscopically material from 64 cases of leucoplacia, 39 of which had cancer. Occasionally, variations were seen in the sections from the same case, but in general the picture corresponded to the stage of the disease. He describes his findings under a hyperplastic and an atrophic stage. In the former there is an extensive subepithelial leucocytic infiltration, acanthosis, and parakeratosis followed later by a marked increase in the granular layer. A considerable round cell infiltration and hyperemia are found in the connective tissue. Toward the conclusion of this stage, connective tissue and sclerosis increase. As the atrophic stage approaches, there is increasing hyperkeratosis and thickening of the granular layer but a decrease of the acanthosis and round cell infiltration in the cutis, sclerosis becomes more marked. In the typical late stage, Breisky's kraurosis, there is considerable hyperkeratosis, a thin granular layer, absence of papillæ, and atrophy of the epidermis. In the cutis, the round cell infiltration is less marked, being in circumscribed lymph zones. Mast and plasma cells are present. In many areas just beneath the epithelium, the connective tissue undergoes a peculiar collagenous change so that the upper part of the dermis has a glary appearance and contains only a few normal cells. The elastic tissue, even in the earliest stages of the disease, always showed some decrease in amount between the epithelial papillæ and directly beneath the basement membrane. This decrease became more and more marked with advance of the disease, until it was completely lost. In the lower portion of the cutis it appeared to be dislodged and disintegrated.

*B Scleroderma circumscripta.* There are two main varieties of circumscribed scleroderma, (1) Morphea which is characterized by variously sized plaques, lines or bands which are slightly elevated or depressed and are surrounded by a violaceous or a violet tinted halo. These patches may reach the size of several inches in diameter. The central portion is usually quite hard, infil-

trated and lardaceous, and has a whitish, yellowish, or old ivory hue. (a) Card-like scleroderma of Unna and white spot disease.

Through the investigations of Montgomery and Ormsby MacKee and Wise, Wise and Rosen, and others, it is claimed, although there have been opinions to the contrary that the cases described as white spot disease are examples of either circumscribed scleroderma or lichen planus sclerosus and that card-like scleroderma is identical with the former group. While morphea usually shows the same histology as diffuse scleroderma, a considerable variation has been met with in the card-like and white spot cases. Although some of them present histological changes in the skin similar to ordinary scleroderma, others have shown degenerative changes in the collagen and elastic tissue not commonly met with in diffuse scleroderma and morphea. Such variations, however have been found in different lesions in the same case which has led to the belief that they represent merely steps in the evolution and development of the diseased process. The finding also of these white spots in association with diffuse scleroderma and morphea has further supported the presumed identity of the conditions.

The clinical appearance of this form of circumscribed scleroderma has been described by MacKee and Wise as follows: "White spot disease occurs mostly in females, especially in those of a neurotic temperament (according to Pettes, in those with a tuberculous taint). It may occur in childhood or in early and late adult life. Most of the recorded cases were in the third or fourth decade. The disease is essentially chronic in its course, the lesions making their appearance insidiously and developing slowly. Aside from the moderate pruritus, especially in the beginning, subjective symptoms are rare. The areas of proliferation are at the base of the neck, in front and behind, the upper portion of the chest and back, but the lesions may appear on the extremities, various portions of the trunk, on the genitals, etc.

The essential lesion is a small white spot. The color may be snow white, ivory white, mother-of-pearl, bluish white, etc. The lesions may vary in size from a large pin-head to a dime. They may be isolated, sparse and widely scattered, or they may be numerous, grouped and confluent. The

surface may be smooth or wrinkled, glistening or dull, depressed or slightly elevated, or level with the surrounding skin. There may be a raised edge and a (relatively or actually) depressed center. The entire surface of the lesion may be uniform in color and consistence, or there may be a peripheral band which is bluish, reddish, or lilac in color. Sometimes fine blood vessels may obtain at the edges. The individual spots are usually round, oval or polygonal in shape, sharply circumscribed, and having the appearance of being imbedded in the skin, like a mosaic. The integument surrounding the lesion is normal. The spots may or may not be perifollicular; some of them may be pierced by a hair or by several hairs or they may contain one or more horny plugs.

"To the palpating finger the lesions may be imperceptible or they may impart a sense of resistance (induration) or they may feel exactly like the normal skin, or appear to be even softer than the normal skin.

"In some of the cases the lesions were somewhat scaly. In others, the superficial portion of the entire lesion could be picked out of the skin with the finger nail, disclosing a reddish-white bed beneath, sometimes showing fine blood vessels. Vigorous rubbing would detach a scale in certain instances leaving the deeper portions intact. Atrophy appeared to be a prominent feature in some of the cases. In others, nothing suggestive of atrophy could be discerned.

As previously noted, considerable variation has been met with in the histology of white spot scleroderma. The collagenous tissue has usually shown hypertrophy with a more or less homogeneous or glassy appearance, degenerative changes, or sclerosis. Varying degrees of inflammatory reaction and cellular infiltration have been described. The elastic tissue has been found to be normal, decreased, or entirely absent in certain areas. The epidermis is usually atrophic with some hyperkeratosis.

Unna, in the material from his two original cases of card-like scleroderma, thought he was able to delineate histologically the various stages of evolution of the disease. In the early stage, the pathological process affected the papillary bodies and an adjacent portion of the cutis proper in the form of a sharply margined flat patch. There was an interstitial edema, swelling up of the collagenous fibers, and the connective tissue cells were increased in number. The lymph and blood vessels were dilated and around the edge were volum-

Some cases in this group have also been described as morphea papulosa. It is pointed out that this descriptive term is misleading. As to the so-called white spot disease which is considered that all cases reported on such are presumably examples of papular scleroderma, not, as is often assumed, true that all cases of scleroderma papulosa are portions of white spot disease, in the clinical sense. As stated, white spot disease differing but not other reasons and as yet confined to lichen sclerosus. We are unable to understand that white spot papulosa and possibly gray scleroderma of ordinary scleroderma papulosa are relatively common, those of true white spot disease are rarely encountered.

As the nomenclature of the term white spot scleroderma, used in relation of this variety is according to Unna, card-like scleroderma and the cases of white spot disease belonging in this category. It is to be noted, however, that

mous collections of spindle and small round cells. There was no increase or hypertrophy of the collagenous or elastic tissues. The latter was reduced in some places. In a later stage the collagenous tissue was much more homogeneous, appearing like a firm collagenous plate and the cellular infiltration had partly disappeared. The vessels were greatly narrowed and decreased in number and the elastic tissue was thin and atrophic and had disappeared in places. In a further stage of development, no cells whatever, with the exception of a few naked nuclei, were to be found in the collagenous patch, but at the border there were isolated cellular collections. The vessels had disappeared but a few groups of elastic fragments were present. The epithelo-cutis margin was broken up by irregularly formed lymph spaces.

Westberg, who first described white spot disease, reported a marked hypertrophy of the collagenous bundles which stained intensely with polychrome methylene blue assuming more of a violet than a bluish color. With Van Gieson's stain also, the staining of the affected tissue was more intense than the surrounding connective tissue and the color was more yellowish than red. The elastic tissue was preserved.

Johnston and Sherwell found that the collagen had altogether disappeared, being replaced by a granular material which had lost its characteristic acidophilic staining tendency. The elastic tissue was broken up into short lengths or granules and the network covering the papillæ had disappeared where the process was most advanced.

In Hazen's case, there was a sharply circumscribed area involving about one-half of the depth of the cutis in which the collagen had undergone marked rarefaction and degeneration with an almost complete disappearance of elastic tissue. Only a few stray cells were found in the degenerated area.

Ward examined two lesions from his case, one considered early and the other in a later stage. In the first there was an increase in the connective tissue cells and what seemed to be a new formation of young connective tissue filling up the lymph spaces. Elastic tissue was well preserved. In the older lesion there was hypertrophy of the collagenous tissue with the disappearance of the cellular infiltrate from the body of the lesion. The elastic tissue was still present but was atrophic.

Hoffmann and Juliusberg reported a uniform structure of the connective tissue in which there were elongated cells lying horizontally or forming a network. There were no thick bundles as in normal connective tissues. The subepithelial elastic tissue was absent, but a little lower down

it was increased in amount. Still further down however, at the margin of the infiltrate, it was markedly decreased and entirely absent in some areas.

Riecke found increased density of collagen with intact elastic tissue, and Petges a connective tissue thick, dense, compressed, and somewhat homogeneous.

In Kretzmer's Case 1, the connective tissue fibers were thin, stained poorly, and contained few cells. In Case 2 (clinical history of bullæ) the connective tissue was cell free with no elastica.

Montgomery and Ormsby reported 2 cases. In the first one an early small lesion showed a hypertrophic and somewhat homogeneous collagen with little tendency to interlacing of its fibers. The elastic tissue was absent or represented only by small bits here and there. In the second biopsy from the first case taken from the edge of a larger lesion, the collagen appeared as long, straight, fine bundles and fibrils with almost complete absence of elastic tissue. In the second case, the collagenous bundles were comparatively thick and hypertrophic, straighter than normal, and showed little interlacing. Elastic tissue was normal but disarranged.

MacKee and Wise studied two biopsies from their case. The first lesion showed an area of colliquative degeneration or necrosis where the tissue elements were no longer discernible. In some of the sections, a large subepidermic cavity occupied by a homogeneous mass containing a few cells was found in the center of the degenerated area. In the second biopsy, the connective tissue was dense with large, coarse, wavy fibers. The elastic tissue was present directly under the epidermis with an area beneath, however, in which it was absent or badly fragmented, lower down in the section it again appeared practically normal.

In a second case reported by Wise and Rosen, edema and swelling of the collagenous tissue was found in the early stage. Later the papillary bodies appeared as homogeneous, or occasionally granular, red staining masses with loss of staining affinity, and a notable reduction in the number of capillaries and cellular elements. The collagen in the upper part of the reticular layer showed marked alteration in places. The bundles had lost their outlines, were fragmented, giving to the whole a reticulated or mesh work appearance. The blood vessels were few in number and showed constriction of their lumina. In the terminal stage, the cutis was occupied by sclerotic bundles of collagen, poor in cellular elements. Little change was seen in the elastic tissue.

Payenneville and Cailliau report 7 cases showing variable changes in the collagenous and elastic tissues. Although some of them were quite useful clinically they all showed histologically a common evolution toward scleroderm.

#### REPORT OF CASES

**CASE 1.** Kluwe and white spot scleroderma. Patient was housewife, white, aged 5 years. She had not been particularly robust as child, and her mother always spoke of her as the sick one of the family. She does not remember, however, any particular illness of importance. Her menstrual periods began at the age of 13 years, lasted about 5 days and were associated with good deal of pain. She usually had little whitish discharge, dry before they appeared, but was never troubled with any chronic condition of this character. She was married at the age of 5, and a few years later had some kind of a rash which was called scarlet fever. It was mild, however, and she was confined to the house for only 3 days. Her first child as born a year after her marriage, dying at the age of 3 with what the doctors called wasting disease. Three years afterward, another child was born, and the third one came 7 years later when the patient was 37 years of age. This child died at the age of 4 with heart trouble and diabetes. Her second child is now living and well. All of her pregnancies ran normal course, and she had no unusual trouble during confinement. Her menopause came at the age of 47. She feels that her health was moderately good during her married life until after her last child was born. At this time she began to have some pain in her side and the lower portion of her abdomen. A suppression of the ordinary removal of the appendix and the right ovary was done in 9. She was then 39 years of age, and felt better for 6 or 8 months after the operation. The pain, however, returned, and it has bothered her off and on since. It was mainly for this reason that she came to the Gynecological Department of the Johns Hopkins Hospital. Her marital relations were not attended with any unusual incidents except that they precipitated attacks of itching. About 3 years ago, however, she began to have a feeling of constriction in the vagina, and made then any attempt at intercourse has been painful.

Patient's first recollection of any changes in her skin are white spots on her wrists, but she was about 3 years of age. Her mother, however, had apparently noticed them before and said that they were due to rheumatism. It was not until about 10 years ago, however, that her attention was called to the one on the back of the right hand, and the one on the back of the left thigh, the latter caused a little itching but the others, with the exception of those around the buttocks and genitalia, have produced no subjective symptoms.

Itching was first noticed when she was 8 years of age at the time menstruation started. Each period would be accompanied by more or less severe pruritus which would stop promptly after menstruation ceased. The itching would at times be so intense that she would become almost frantic. The attacks continued at the same intervals after her marriage but would also frequently follow sexual intercourse. After her last child was born, when she was 37 years of age, the itching became much less intense and did not bother her very much until about 3 years ago. At this time she began to note some soreness around her anal region, which was at times so uncomfortable when she was sitting down, that she would have to use cushions. This was year or more after the menopause. Pruritus became very annoying again and extended back around the anal

region. She would have one or more attacks during the day and often several during the night, which disturbed her so that she could not sleep. She also had drawing, dry forcing around the vagina and would frequently have the sensation of something coming out of the vaginal opening but seldom found anything to account for it.

Patient was first seen in the gynecological dispensary in July 1932, and was later examined in the gastro-intestinal department. Her chief complaints then were constant feeling of pressure in the right lower quadrant, backache, and pain in the rectum during defecation.

On examination, no important changes were found in the general physical examination. She was slightly anemic. The blood count was 10,000 and phosphorus 4.5 milligrams per cent. A last meal showed free hydrochloric acid, of total acidity 8. X-ray examination revealed no elastic stomach, right lower quadrant adhesions, and four small stones in the gall bladder. The urine contained traces of albumin, a few red blood cells, and many white blood cells, but in a centrifuged specimen only a few white cells were present. Cultures showed bacillus coli. Cytoscopic examination was negative. At the exception that several catheterizations showed some obstruction to the apex of the left broad ligament. The following supplementary tests were made for us later through the kindness of one of the gynecologists. The external genitalia shows numerous lesions of the skin. The labia majora are not atrophied or sclerosed, but there is some loss of elasticity. The labia minora have disappeared and the clitoris can no longer be seen. There is small urethral caruncle present. At the fourchette there is a marked area of leucoplakia, and there is some constriction of the vaginal orifice. The perineal has small rectocele. The mucous membrane of the rectosigmoid is freely movable, and apparently the walls of the vagina show no evidence of leucoplakia or loss of substance at times. The cervix is normal. The uterus is of normal size and in good position. The adnexa are normal. The tissues around the posterior part of the vaginal orifice are very tender.

The patient was seen first in the skin department in July 1932. The small labia had entirely disappeared and only stump of the clitoris remained (Figs. 1 and 2). The skin on the inner surfaces of the large labia extending down over the perineum and around the anal region was dry, somewhat stiffer than normal, having grayish or thin milk color with here and there small reddish inflamed patches and occasionally pigmented spots. Around the clitoral stump, the fourchette and in some other locations near the vaginal opening, it had the crumbly thickened, mottled appearance characteristic of patches of leucoplakia.

In the intergluteal fold, around the perineum and the thigh folds, there were numerous pea to quarter of dollar sized chalky white, well defined somewhat irregular patches, most of which were slightly elevated and indurated. One large patch involving most of the left side of the intergluteal fold, extended out over the crest of the buttocks, its outer edge was little raised, only wrinkled, and had a milk white color. On the other side there were numerous smaller lesions, some of them confluent. Near the anal opening the skin was somewhat pigmented, thickened and smooth, showing no definite whitish patches similar to those further out, and none of this same character could be identified on the inner surfaces of the large labia.

On the inner surfaces of both wrists, there were dozen or more pea-sized to split pea sized whitish papules similar to those around the genitalia. Some of them were slightly raised, others little depressed or cup shaped. The surfaces were smooth or showed few punctate depressions.



Fig 1



Fig 2

Fig 1 Case 1 White spot scleroderma associated with changes resembling kraurosis vulvæ. The whitish papules and patches around the vulva and perineal region were definite lesions of white spot scleroderma, but we did not find the typical connective tissue changes in the specimens taken from the inner side of the large labia.

Fig 2 Case 1 Typical lesions of white spot scleroderma on thigh and extending out over crest of the left nates

They were round or irregular, discrete or confluent. The skin between the papules was slightly pigmented and showed some small, irregular, atrophic depressions. There were a few similar spots on the backs of the hands and on the arms, some of which were linear in shape. On the back of the right thigh, near the popliteal space, the largest of the individual lesions, with the exception of the patch on the buttocks, was found. This was about 3 centimeters in diameter, was moderately elevated, and quite scaly.

During several months that the patient was observed in the dispensary, none of the lesions ever showed any redness or other signs of inflammation, with the exception of the large patch over the left side of the buttocks and the one on the back of the right thigh. The former would often have a pinkish tint and seem to be more elevated than usual, while the latter became infected following a bruise. A superficial ulceration formed over the central portion with a surrounding redness stopping abruptly at the edge. At one section of the periphery, the epidermis was undermined by a serous, clear fluid. Under appropriate local therapy the infection healed after 2 or 3 weeks, leaving a moderately thickened, red scar showing little evidence of the original condition of the skin.

Histological examination. Four specimens of skin were taken from various locations. The tissues were fixed in Zenker's fluid to which 25 per cent of a 10 per cent formalin solution had been added. Sections stained with hematoxylin and eosin and Verhoeff's elastic tissue stain with a Van Gieson counter stain were depended upon mainly for the histological study, although various other methods were used.

Specimen 1. This included in its entirety a lesion on the arm 1 centimeter in diameter, which was smooth, white and glistening, and showed no clinical evidence of any inflammatory reaction. In the papillary layer and the upper portions of the reticular layer, a well defined area was found in which the collagenous fibers appeared to have been pulled apart with loss of substance, into interlacing, wavy fibrils running in various directions (Figs 3 and 4). In some locations these fibers formed a lace-like network with spaces in between, which were either clear or contained a finely granular or amorphous material. In other loca-

tions, the bundles seemed to be welded together into a more or less structureless mass. The affected portion of the cutis stained less intensely with eosin than the more normal layers beneath. Scattered among these fibrils, there were a few small, dilated capillaries and an occasional, well preserved, small round cell or larger mononuclear. The affected area gradually merged into the surrounding more normal portion of the cutis.

Elastic tissue fragments were rather numerous in the subpapillary layer of the dermis, but were completely absent in the lower portion. Around the edge of the lesion there were frequently rather large collections of cells which extended down into the fatty layer. These cells appeared to be mostly lymphocytes, but an occasional plasma cell was found. No notable changes were observed in the deeper blood vessels. Sweat glands appeared to be normal. The epidermis was atrophic with a loss of the rete pegs, and there was a moderate hyperkeratosis.

Specimen 2. This tissue was removed from the inner side of the buttocks near the perineal region. The cutis was occupied for the most part, by rather dense, fibrous tissue. Most of the bundles were fine and wavy but in one or more locations, they appeared to be hypertrophied, and had a somewhat glassy appearance. There was a rather dense cellular infiltration, particularly marked in the upper portion of the cutis which occurred in variously sized masses as well as rows between the connective tissue bundles. These cells were mostly of the small, round type, but there was an increase in the connective tissue cells and numerous plasma cells were present especially in the deeper layers. In one area a group of giant cells were seen which apparently surrounded the remains of a hair follicle and, in another location, there was a deposit of calcium (Fig 5). At one end of the section, the upper portion of the cutis was occupied by a large, relatively clear space from which most of the connective tissue fibrils had disappeared. It showed a very fine reticulum containing, in most of the meshes, some fine granular material, a few cells, and some dilated capillaries. Numerous red blood cells were seen in certain areas just under the epidermis (Fig 6). Around the border of this zone there were dense collections of cells, and the elastic tissue was compressed





Fig. 3



Fig. 4



Fig. 5



Fig. 6



Fig. 7



Fig. 8

Fig. 3 Case. White spot scleroderma. Specimen 4. Hematoxylin and eosin stain. From small lesion on the arm. Splitting up of collagenous bundles; decrease of connective tissue nuclei and blood capillaries.

Fig. 4 Edge of same lesion as in Figure 3. Elastic tissue stain. Note relative lack of inflammatory reaction at spreading (?) edge of papule.

Fig. 5 Case. White spot scleroderma. Specimen 4. Perineal region. Elastic tissue stain. Hyperkeratosis, diffuse cellular infiltration, sclerosis, and calcium deposit.

Fig. 6 Same section as in Figure 5. Hematoxylin and eosin stain. Rarefaction of connective tissue similar to that found in lesion from arm (Figs. 3 and 4).

Fig. 7 Same section as in Figure 5. Elastic tissue stain. Hyaline blocks in subpapillary zone; compression in some areas and loss in others of elastic tissue.

Fig. 8 Case. White spot scleroderma. Specimen 4. Inner side of large labial. Hematoxylin and eosin stain. Moderate hyperkeratosis and thickening of epidermis. No striking degenerative changes in connective tissue.

In another location the tissue immediately under the epidermis had become homogeneous, forming glassy hyaline block (Fig. 7). The elastic tissue appeared dense and compressed over most of the sclerotic area, but in certain locations it was entirely absent. It had also disappeared from the clear area seen in Figure 6, and the hyaline blocks in Figure 7. The blood vessels throughout the sclerotic area were numerous and dilated but showed no important changes. Portions of hair follicles were observed here and there. The epidermis showed loss of most of the rete pegs and was thickened in some areas. There was considerable hyperkeratosis.

Specimen 3. This specimen was removed from the outer edge of the lesion on the left side of the buttocks. Here the entire upper part of the cutis as occupied by relatively clear areas similar to that previously described as one portion of Section. Elastic tissue fragments and splintered bundles extended up into the lower portion of this area looking as if they had been pulled up by some sucking force in the upper zone. Some of the small blood vessels in the

narrowed area had thickened hyaline walls. In the deeper layers, there were dense collections mainly of small round cells with, here and there, few giant cells. The elastic fibers were disarranged and in some areas swollen and fragmented or degenerated. The epidermis was quite atrophic, but there was some hypertrophy of the lower layer which was made up of thin, loose bundles.

Specimen 4. This specimen was removed from the inner side of the labia majora extending from near the stump of the clitoris over toward the outer margin. The cutis was occupied by moderately fine, branching connective tissue which, in some areas, was rather dense and relatively poor in cells, while in others it was more loosely located (Fig. 8). There was scanty diffuse infiltration of cells, most of which resembled connective tissue cells, but few lymphocytes, plasma cells, eosinophils and large mononuclears were seen. The elastic tissue had disappeared from the papillary and subpapillary portions of the cutis. The epidermis was definitely thickened, with moderate hyperkeratosis and in some areas showed considerable prolongation of the rete pegs.

**CASE 2 White spot scleroderma** Patient was a white woman, aged 56 years. The condition had been present for 2 years. Over and underneath the breast were numerous pea to fingernail sized, roundish or elongated chalky white patches which had become confluent in certain locations (Fig 9). Some of the lesions were a little depressed and most of them were scaly. One showed dilated capillaries on the surface, and this one was removed for histological study.

The appearance of the sections from this patient was identical with those obtained from Case 1. In some locations the same relatively clear areas (Fig 10), with lacunæ containing degenerated red blood cells, were found as previously shown in Figure 6. Surrounding these areas, and also in certain other locations between them, the collagenous tissue had the homogeneous, wavy cell free aspect shown in Figure 3 (Fig 11). In other sites it was of a rather dense fibrous type. The elastic tissue in the lower portion of the cutis was swollen, broken up and disarranged, often forming large twisted hundles. There were several large collections of lymphocytes with plasma cells here and there.

**CASE 3 Morphea** A white woman, aged 33 years, presented a leathery smooth patch 3 by 8 centimeters over the back of the neck, which had been present for 6 months. It had a pinkish border which was surrounded by a pigmented zone. The biopsy specimen was taken through the edge of the lesion so that it contained some of the normal skin.

In the clinically normal portion of the section there were no changes, except a dilatation of the capillaries and a mild perivascular infiltration, with some increase of the pigment cells both in the cutis and the basal layer of the epidermis. As one approached the center of the section, especially in the deeper portion of the cutis, the collagenous bundles became larger and more homogeneous in appearance, there was a decrease in the blood vessels, and the connective tissue cells were compressed. Still further toward the center, the connective tissue gradually assumed a rarefied, wavy, relatively cell free appearance (Fig 12). The elastic tissue had, for the most part, disappeared in the rarefied area, and was decreased in the papillary and subpapillary layers in most of the section. In the lower portion of the cutis, it appeared fragmented and in some areas diminished.



Fig 9 Case 2 White spot scleroderma Lesions on breast.

The epidermis was atrophic showing a mild hyperkeratosis over the inner portion of the section.

In the 4 other cases of morphea studied, none of the areas of rarefaction of the collagenous tissue were found. This tissue showed either hypertrophy or atrophy with variable changes in the elastica, such as are more commonly met with in morphea and diffuse scleroderma.

**CASE 4. Leucoplacia** Patient was a white woman, aged 64 years, who had complained of itching for 2 years. Menopause occurred 20 years ago. The external genitalia showed a loss of elasticity and subcutaneous fat, consistent with the age of the patient. The clitoris and labia majora were well defined. The labia minora were atrophic but could be identified. On the inner surfaces of the labia majora and extending to the introitus, there were well defined, white areas varying in size from 0.5 to 1 centimeter which tended to be confluent. They were slightly indurated but showed no secondary changes. The introitus was not constricted.

The section apparently was cut through the specimen across the labia majora at right angles to the vaginal opening, since on one end hair follicles and sebaceous glands



Fig 10 Case 2 White spot scleroderma Elastic tissue stain. Thinning out of connective tissue. Formation of lacunæ, some of which contained red blood cells. This lesion had probably been traumatized, since it was the only one in the group that showed dilated capillaries or blood spots on its surface.



Fig 11 Same specimen as in Figure 10. Hema toxylin and eosin stain. Does not show open spaces as seen in Figure 10, but masses of red blood cells are present in the subpapillary layer and there is a separation at the dermo-epidermal junction. Note resemblance to Figure 3 of Case 1.



Fig. 3. Case 3. Morphia. Elastic tissue stain. Rarefaction of connective tissue and loss of elasticity.

were present. Throughout the greater portion of the cutis, the collagenous tissue had been replaced by a lightly stained homogeneous or granular substance lying in fine reticular net work (Fig. 1). Some areas are cell free, while in others both connective tissue and small round cells are quite abundant with, here and there, an occasional eosinophil and chromatophore. There were few dilated blood vessels with well preserved walls, and just under the epidermis some spaces containing red blood cells. One end of the sections, where the sebaceous glands and hair follicles are present, the connective tissue was quite cellular and showed some diffuse round cell infiltration. The curiously altered collagenous tissue gradually blended into the loose or less normal appearing bundles in the lower half of the cutis, here the blood vessels were dilated, but showed no notable changes elsewhere. There was good deal of edema and cell infiltration in the lower part of the cutis and most of the elastic tissue had disappeared. A very few elastic fibers could be seen anywhere in the papillary layer. There was moderate degree of hyperkeratosis over most of the sections, with little thickening of the epidermis in some areas and an atrophy in others.

**CASE 5. Leucoplakia.** Patient was white woman aged 60 years, who had been operated on for carcinoma on the left side of the labia, which was surrounded by large area of leucoplakia. No history of itching.

Surrounding the carcinomatous area, there was marked hypertrophy of the epidermis with an extreme thickening of the horny layer, most of whose cells contained shrunken nucleus and many of them granular. The granular layer was quite thickened and in some areas as wide as the rete itself. There was rather marked diffuse cellular infiltration of the cutis and in few locations in the subpapillary layer the collagenous tissue was rather dense, contained few cells and had hyaline appearance. Very little elastic tissue was seen in the papillary and subpapillary layers. I another section taken through the lower portion of the gross specimen below the carcinoma, the connective tissue in many places was quite loose wavy and devoid of cells. In other locations it was denser and preserved, and showed some irregularity in staining with eosin. Considerable cellular infiltration was noted in some part of the cutis. Elastic tissue had, for the most part, disappeared in the papillary and subpapillary layers. In most of the sections the epidermis was atrophic, with the keratin, and moderate hyperkeratosis in one or two areas.

**CASE 6. Leucoplakia.** Patient was a white woman, aged 24 years, who had complained of itching of the vulva for



Fig. 4. Case 4. Leucoplakia. Elastic tissue stain. Marked rarefaction of connective tissue, partial preservation of small blood vessels, atrophy of epidermis.

4 or 5 years. The following set was taken from the labia. The external granulation has undergone marked changes. There is a very definite loss of subcutaneous fat. The labia minora are shrunken and the folds of the clitoris have become adherent over the clitoris so as to hide it completely. The labia majora are also shrunken, and numerous fissures are present. The gross pathological set stated that the skin appeared normal, except for few small, brown patches on the skin, which are apparently leucoplakia.

Three pieces of tissue are available for study from the external set. In two of these specimens, in some locations, the connective tissue in the upper half of the cutis had the same coarse appearance, which has been previously described, except that it was more dense and homogeneous (Fig. 2). In other locations it was finely woven together and diffusely infiltrated with small round cells and occasionally other types. In the lower portion, there were dense collections of lymphocytes with some plasma cells and eosinophils. Elastic tissue was absent for the most part, in all of the specimens in the upper third of the cutis. The epidermis showed hypertrophy in few locations but in general was slightly atrophic with certain irregularities in growth. In most of the sections the pruritus apparently occurred in the apical opening showed rather marked parakeratosis with few areas of hyperkeratosis.

**CASE 7. Leucoplakia.** (Gross macroscopic sets alone available). The specimens consisted of a large area of tissue that had been removed from the upper part of the vulva, including the clitoris, which was represented by a small, irregular stump. Over the surface posterior to small split pin suture marks spots were scattered, which were mainly, irregular or elongated shape with comparatively normal looking skin between. There was definite thickening and hyperkeratosis of the tissue around and over the clitoris and also the medial portion of the specimens toward the lower border.

Two sections were taken for histological study one across the top running through the clitoris and the other across the lower portion of the specimens. In both sections there was rather marked hyperkeratosis with hypertrophy of the epidermis in some areas but in other locations it was thin and atrophic. There was rather diffuse cellular infiltration with many eosinophils throughout the cutis. Each showed marked edema with nicely dilated



Fig 14 Case 6 Leucoplacia Elastic tissue stain Homogeneous melting together of connective tissue, loss of elastica Hyaline changes around blood vessels Parakeratosis



Fig 15 Case 7 Leucoplacia Elastic tissue stain Rarefaction of connective tissue. Hyperkeratosis

capillaries. In some locations, the connective tissue was represented by a loose network of fibrils and a homogeneous ground substance, which contained a few cells and widely dilated capillaries (Fig 15). The elastic tissue had, for the most part, disappeared in the upper half of the cutis.

CASE 8 Leucoplacia. White woman, aged 55, had complained of itching and burning of the vulva, particularly after urination, for 3 months. She had had no previous skin trouble. Gynecological examination was negative except for the local condition. The vulvar tissues were soft and moderately atrophic. The skin on the inner sides of the labia was red, slightly thickened, and had a dry, parched appearance. The clitoris was retracted, being represented by a navel like pouch, and the surrounding skin had a chalky whitish appearance. In the medial line, above the clitoris and also along the midline of the perineum, there was a superficial fissure formation with some whitening of the skin around the side. The labia minora had completely disappeared, and the skin around the anus was slightly reddened. A partial vulvectomy was done, and tissue for microscopic study was taken (1) across the fissured red area about 2 centimeters above the clitoris, (2) through a small fissure on the inner side of the vulva near the perineum, (3) across the stump of the clitoris.

In the first specimen, there was a considerable thickening of the epidermis, and a hyperkeratosis toward the center of the section which gradually decreased in amount as one approached either end. There was a dense cellular infiltration in the upper portion of the cutis most marked also, toward the central portion of the section. The second specimen was similar to the first, but here the epidermis was somewhat more thickened except at the location of the fissure, where it had completely disappeared. In the third specimen, there was a little thickening of the epidermis, with a moderate hyperkeratosis toward the ends of the preparation, but as one approached the central part which represented the remains of the clitoris and the immediate surrounding portion, one encountered a striking homogeneous, hyaline appearance of the cutis most marked around the small blood vessels some of which were completely occluded. This area contained only a few nuclei and the overlying epidermis was atrophic (Fig 16). The elastic tissue had disappeared for the most part, in the upper portion of the cutis in all three preparations.

CASE 9 Leucoplacia. A white child aged 8, complained of pain after urination, itching of vulva, and bed-wetting, of 3 years' duration. This child had been studied in the Harriet Lange Home for some time, principally as a behavior problem. She rubbed her vulva a great deal, and one could not determine whether the primary urge was mainly itching or masturbation. Gynecological examination was negative except for the local condition.

The tissue of the vulva was soft, and there was no evidence of any diffuse sclerosis. The skin on the inner sides of both labia was thickened, and had a smooth white appearance (Fig 17). The process involved the whole surface from the clitoris to the fourchette. There was some inflammatory reaction and maceration around the perineum and anal regions.

A section was taken through the edge of the diseased process on top of the labia. Normal appearing hair follicles and sweat glands were present throughout the entire specimen. In some areas there was a considerable thickening of the epidermis with a marked hyperkeratosis. In other locations the epidermis was atrophic with flattening out of the rete pegs. In most of the section the upper

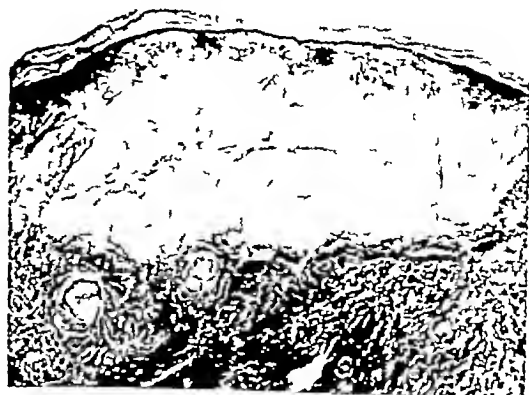


Fig 16 Case 8 Leucoplacia. Elastic tissue stain. Homogeneous connective tissue and hyaline changes around blood vessels resembling particularly Figure 14. Atrophy of epidermis

resulting in a dissolution of the fibrils, we do not know. We do feel, however, that the process is not due to simple edema, whether of the nature of a transudate or exudate, but that there is some primary fundamental disturbance in the protoplasm of the connective tissue itself. It is quite possible that the degenerated collagen could act as a foreign body and provoke a secondary restitution granulation tissue, as Terruhn believes, but in white spot scleroderma at least the lesions, when not subjected to irritation, may persist for years without showing any evidence of inflammation or secondary sclerosis.

We have made several other stains such as Masson's trichrome, Mallory's aniline blue, poly chrome methylene blue, a silver stain, and some bacterial stains, besides those already enumerated. In general, the degenerated connective tissue stained in a similar manner although often paler to the finer collagenous fibrils in the papillary bodies. Occasionally especially around the capillaries in the affected areas, the tissues had a hyaline appearance but we found little evidence of fibrin in the rarefied areas.

In some of our sections lacunae or open spaces containing little or no demonstrable substance were often seen. These were due, we believe, to a tearing apart of the tissues from operative procedures or other injury. The lack of cohesiveness in these areas is well illustrated in the histological material from all of our cases, in which there was always a tendency to a separation at the epitheliocutis margin.

While it is generally conceded that white spot scleroderma is apparently a disease primarily affecting the collagenous tissue of the cutis it is more difficult to interpret the significance of these changes in kraurosis of the vulva. Two or more possibilities may be mentioned ( ) that leucoplasia of the vulva is not a specific entity but may be the expression of various diseases modified in appearance by their location. Thus, Oppenheim states that neurodermatitis, lichen simplex chronicus, lichen planus, scleroderma, and chronic vulvitis are often thrown into the group of kraurosis vulvae, although he believes that Breslay's kraurosis is a separate clinical entity. It seems quite likely that white spot scleroderma may affect, in some cases, only the genitalia where the individual lesions could very well intimately resemble a plaque of leucoplasia or through fusion and secondary sclerosis from irritation, Brelslav's kraurosis ( ) It may be argued that the connective tissue changes characteristic of white spot scleroderma (our 3 cases at least) represent only an accidental incident in the pathology of kraurosis

vulvae. We must confess that this would have been our interpretation had we not been able to compare the histological material of Case 1 from the arm, with that around the anal region where the inflammatory reaction and secondary sclerosis were prominent features. Here, without doubt, trauma and other irritation incident to location were responsible to a considerable degree for this complication.

With reference to the whole subject we can only point out that a considerable proportion of cases classified as kraurosis vulvae or leucoplasia are associated with peculiar connective tissue changes similar to those found in our cases of white spot scleroderma. Because of the conflicting opinions concerning the two former affections, both clinically and histologically we believe, as expressed by Oppenheim, that several diseases involving the vulva have at times been reported as examples of kraurosis or leucoplasia. It is very likely however that there may be a true primary leucoplasia of the vulva in the pathological sense (marked hyperkeratosis and acanthosis) and also that the process may be secondary to other affections just as is the case for example, in the mouth after syphilis and lichen planus. It is quite evident that many cases of whitish patches on the vulva, which have been called leucoplasia, were not a real leucoplasia in the histological sense, and in our own material only Case 4 showed a striking hypertrophy of the epidermis which is limited to the tissue immediately surrounding the carcinoma.

The frequency however with which cancer develops on these vulvar lesions demonstrates the strong tendency to epithelial proliferation in this location, and external irritation and a special susceptible soil are undoubtedly important contributing factors.

Our Case 9, a child 8 years old, presented clinically the picture of a diffuse leucoplasia of the vulva, although there was hardly sufficient hypertrophy of the epidermis to support this diagnosis in the histological sense. In the cutis, however, the connective tissue showed degenerative changes resembling those which were found in our cases of white spot scleroderma and leucoplasia. We have classified it temporarily with the leucoplasias in the clinical sense principally because of the location of the lesion. We have encountered nothing like it before and Dr. Leo Brady who has had occasion to observe a great variety of gynecological affections in children especially various types of vulvitis from infection, incontinence of urine, masturbation, etc. tells us that it is unique in his experience.



regard this region as site of predilection for scleroderma, especially in elderly women. The microscopic findings described by Ketrón and Ellis may prove definite step toward the elimination of such confusion regarding kraurosis and leucoplasia, but I cannot entertain the same view with respect to scleroderma and white spot disease, when these occur on the genitalia.

While I fully appreciate the significance of their microscopic studies relating to degenerative changes in the connective tissues, in their various sections, I have the impression that the histological changes found in diffuse scleroderma, morphea and white spot disease are sufficiently definite to permit their differentiation from other diseases clinically resembling them. As to kraurosis and leucoplasia, I would hesitate to accept the idea of regarding them as one and the same disease, even in cases in which they co-exist and in which microscopic differentiation is difficult or impossible. It is not hard to conceive that different evolutionary stages in both diseases may at times resemble one another very closely both clinically and microscopically. It must be borne in mind that leucoplasia has tendency to become leukokeratosis, possibly leading to cancer of the vulva, as it does in the mouth, it is true that kraurosis may also eventually in cancer but kraurosis is characterized by definite progressive atrophy quite distinct from the changes peculiar to leukokeratosis with its epithelial proliferation. It appears to me that the differential diagnosis between these various conditions rests largely upon the clinician and I leave the discussion of histopathology to those with much greater experience than I possess.

DR HAMILTON MONTGOMERY, Rochester, Minnesota. The paper was very interesting to me because I recently made clinical and pathological study of differentiation of kraurosis vulvae, leucoplastic vulvitis, and pruritus vulvae, and also because of case that I saw recently at dermatological meeting, which was presented as kraurosis vulvae, but which had typical lesions of lichen sclerosus et trophicus of Hallopeau. Furthermore, in this case there was no true atrophy or tissue of the vulva, such as one sees in kraurosis.

Cases of kraurosis, just now so well defined by Dr. Williams are to be separated from leucoplasia of the vulva and pruritus vulvae with lichenification. Kraurosis rarely leads to epitheliomatous changes, whereas leucoplasia frequently does. It is not unusual, however, to find features of two or all three conditions superimposed in the same individual, especially as all three conditions are prone to occur in the later decades of life. The histological picture of lichen

sclerosus et trophicus and certain stages of kraurosis may be indistinguishable, but this does not necessarily denote the same etiological factors in both diseases. In both there is adema between the epidermis and cuts. The elastic tissue is not destroyed but simply frayed and epitelized and separated from the papillary bodies by thin adema and trabeculae, the latter resulting in leucoplasia of the connective tissue. The histological picture of the cases of leucoplasia, including so called white spot disease, histologically present features of scleroderma and do not show the peculiar band of adema beneath the epidermis, which is the outstanding feature of lichen sclerosus and kraurosis. I am more inclined to believe that at least one, if not two, of Dr. Ketrón's cases are cases of lichen sclerosus with secondary involvement of the labia and have nothing to do with true kraurosis.

DR LLOYD W. KIRKOV, Baltimore, (closing). I am disappointed that Dr. Ware has spent so much of his valuable time justifying the status of kraurosis vulvae as specific entity. We have taken no stand in this argument, but have used the terms more or less synonymously. One could certainly not claim that all cases of leucoplasia are examples of kraurosis vulvae but it seems quite possible, as has been claimed by others, that the latter affection may be merely the end stage of some variety of clinical leucoplasia. As has been previously brought out, I believe that whitish patches on the vulva frequently called leucoplasia, may be produced by more than one pathological process. I am very glad to have Dr. Ware's opinion although it throws some doubt on the correctness of the diagnosis in Case 1. Although some of the lesions presented by this case are much larger than those commonly seen in white spot disease, the clinical appearance of the smaller ones certainly corresponds to this condition and the histopathology is apparently the same as that described by some investigators as characteristic of this affection. The status of white spot disease itself is too insecure to warrant very sharp limitation of its boundaries.

With reference to the remarks of Dr. Montgomery we certainly do not believe that the lesions, particularly on our patient's anus which have been present for many years showing very little tendency to spread, could be due to localized adema. The fundamental process is primary degeneration of the collagenous tissue. An infiltration of serum, however even to the formation of bullae, may occur when such areas are subjected to trauma. This occurred in our Case 2, in the lesions around the buttocks, but we saw nothing of this character associated with those on the anus.

# TRANSDUODENAL RESECTION OF THE AMPULLA OF VATER FOR CARCINOMA OF THE DISTAL END OF THE COMMON DUCT

WITH RESTORATION OF THE CONTINUITY OF THE COMMON AND PANCREATIC DUCTS  
WITH THE DUODENUM<sup>1</sup>

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THE surgical treatment of malignant tumors of the extrahepatic ducts has presented many technical difficulties. The operation of radical extirpation frequently is not applicable by virtue of the location or because of extensive involvement of the lesion, and when possible of execution, it has in the past been accompanied by a mortality rate considerably in excess of that for operable malignant disease elsewhere in the abdomen. Palliative, short-circuiting operations for malignant, obstructing lesions of the common duct have likewise been accomplished with considerable risk, but in the instances of recovery these usually have been justified by the palliation obtained.

The effect on the liver of prolonged obstructive jaundice, particularly as regards disturbance of the hepatic function and reduction of the glycogen reserve, and the effect upon the blood, particularly prolongation of the bleeding and coagulation time, are well known. These have contributed to the increased surgical risk of the jaundiced patient. However, the modern methods of pre-operative preparation of the patient with obstructive jaundice have materially reduced the risk with which surgical procedures on the biliary tract may be executed. The patients with obstruction of the terminal portion of the common duct in which the effects of prolonged obstructive jaundice are manifested are further debilitated by pancreatic insufficiency incident to obstruction of the pancreatic ducts. Lesions in the periampullary region of the duodenum producing both bile and pancreatic retention present formidable surgical problems not only in the technical execution of surgical procedures, but in the control of the various factors contributing to the surgical risk.

While malignant tumors of the extrahepatic ducts may and do occur anywhere from the hilus of the liver to the terminal portion of the common duct, Marshall and others have presented data indicating that nearly one-third of the malignant tumors of the extrahepatic ducts occur in the terminal portion of the common duct, the ampulla of Vater. The infrequency with which malignant tumors in this situation have been surgically extirpated seems to warrant recording the following

case of successful transduodenal resection of the ampulla of Vater for carcinoma of the distal end of the common duct.

## CASE REPORT

The patient, Mrs. M. DeR., 54 years of age, had resided in South America all her life until the past 2 years. On August 15, 1934, at the time of the original consultation, she gave a history of only 3 weeks' duration of epigastric distress and progressively deepening jaundice. The epigastric distress was associated with considerable digestive disturbance, nausea, and vomiting. There had never been any acute pain. There had been no chills but a daily temperature of 100 degrees F. The appetite was poor, and the patient had lost 10 pounds in weight during the short duration of her illness. The patient has recently had some urinary frequency, and some years ago, previous to coming to this country, she was told that she had an enlarged left kidney. At the time of the examination the patient was poorly nourished, weighed 98 pounds, and was deeply jaundiced. The systolic blood pressure was 108, diastolic 70. Examination of the head, neck, heart, lungs, and breasts was negative. Neither the liver nor gall bladder was palpable. A large cystic mass occupied the entire upper left quadrant of the abdomen, extending high under the left costal margin and posteriorly to the kidney region, it was not tender, moved with respiration, and was believed to be an enlarged left kidney, probably a left hydronephrosis. Pelvic and rectal examination was negative. There was no edema of the extremities, and all reflexes were normal.

The patient was admitted to St. Vincent's Hospital for further observation. Urinalysis: specific gravity, 1.010; acid reaction, bile, 4, no albumin, sugar, casts or pus cells but an occasional red blood cell was present. The concentration of the hemoglobin was 60 per cent, and the erythrocytes numbered 3,900,000 in each cubic millimeter of blood. Leucocytes numbered 6200 in each cubic millimeter of blood, and the differential count was as follows: lymphocytes, 36; eosinophiles, 2; basophiles, 1; neutrophiles, 60. The bleeding time was 2 minutes 15 seconds, and the coagulation time was 4 minutes. The renal functional tests, phenolsulphonphthalein and blood urea, were within normal limits. Inasmuch as the renal functional tests were normal it seemed that abdominal exploration to determine the cause of the painless, obstructive jaundice was more important than further investigation of the urinary tract to determine the true nature of the left renal enlargement. A pre-operative diagnosis of obstructive jaundice, probably due to carcinoma of the head of the pancreas, was made.

At operation, August 17, 1934, through a high right rectus incision, it was first determined that the cystic mass occupying the left upper quadrant of the abdomen was a huge hydronephrosis of the left kidney, the right kidney was normal. The gall bladder was greatly distended and the common duct was dilated to about 3½ centimeters in diameter. The liver edge extended just below the costal

<sup>1</sup>Read before the Western Surgical Association, St. Louis, Missouri, December 7-8, 1934.  
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margin. Examination of the stomach was negative. No stones were felt in the gall bladder or common duct. Careful examination of the pancreas disclosed no tumor or abnormal consistency. Upon opening the common duct, several masses of colorless necrotic material escaped. A finger inserted into the common duct downward toward the duodenum encountered freely movable tumor, little more than 1 centimeter in diameter. The ampulla of Vater. The anterior wall of the duodenum was opened, exposing non-ulcerating tumor of the ampulla projecting into the lumen of the duodenum (Fig. 1). The tumor was not adherent to the pancreas but was freely movable. A wide incision of the tumor was made, including the distal common and pancreatic ducts (Fig. 2). The pancreatic duct was about 5 millimeters in diameter (Fig. 3), and when divided liberated considerable amount of retained pancreatic secretion. The medial cut edges of the common and pancreatic ducts were sutured together, and the circumference of each duct was sutured to the mucosa of the posterior wall of the duodenum (Fig. 4). A short piece of catheter was loosely sutured into the pancreatic duct. After the anterior wall of the duodenum was closed, temporary external drainage of the common duct was established by cholecystostomy. The gall bladder was not drained, nor did it seem necessary to establish internal drainage of the gall bladder by any type of splanchnicostomy.

Postoperative course. The patient's convalescence was remarkably uneventful. The drainage from the cholecystostomy tube remained practically colorless for 3 days, following which the bile pigment faintly appeared to become of gross normal concentration by about the eighth day, at which time the cholecystostomy tube was clamped off, diverting the bile into the duodenum, and bile appeared in the stool days later. The cholecystostomy tube was removed on the thirteenth day, which was followed successfully by complete healing without external drainage of bile. The small piece of catheter which had been loosely sutured into the pancreatic duct was passed in the stool on the tenth day. The patient was discharged from the hospital September 5, the twenty-fourth postoperative day, at which time the jaundice had practically disappeared. The patient was presented at St. Vincent's Hospital Conference November 9, in excellent condition, having regained her normal weight.

The pathology of the tumor of the ampulla of Vater removed at operation is described by Dr. John W. Budd. The specimen is an enlarged and bedeviled papilla of V (Fig. 5), which is apple shaped, having base 1 centimeter in diameter and 9 centimeter in thickness, that is capped by hemispherical dome 9 centimeter in diameter. The mucosa of the base and the peripheral half of the dome is intact, but surrounding the masses of the ampulla is an eccentric zone 6 millimeters in diameter which is slightly elevated, pale, spiculate, and ulcerated. The villi have been obliterated leaving smooth non-ulcerated surface. The base of the specimen shows masses of the duodenal wall, with two ducts in cross section into which small probes are readily passed, both probes approximating through common necrosis of the summit of the papilla. The ducts appear definitely dilated and the surfaces presented to inspection are covered by gray soft nodules of tissue. A second specimen which was removed from around the ducts deeper in the duodenal wall, because the cellular tissue was involved in the ducts close to the line of resection, showed normal structures upon subsequent macroscopic examination. A horizontal section through the center of the papilla which included both ducts and the necrosis was embedded in paraffin and sectioned for microscopic study (Fig. 6).

Microscopic pathology. The mucosa of the duodenal folds except for the smoothed-out portions of the dome is

normal. In the latter there is complete replacement of the normal epithelial cells by neoplasia with tubular arrangement still maintained in places but irregular branching almost all more numerous. The replacement is progressing centrifugally, beginning at the summit of the papilla. The mucosa nodules in the right fold are diffusely infiltrated and broken up by neoplastic masses which form long branching tubules. The tumor cells are large and essentially cuboidal although great and bizarre forms are noted. At the base of the papilla the pancreatic duct shows only very narrow margin of normal mucosa before neoplastic epithelium is superimposed on its surface while the common duct shows a greater margin of healthy tissue. The interval between the muscular wall of the two duodenal folds and between the base and the summit of the papilla which is normally occupied by the two ducts and the ampulla, is overgrown and almost wholly replaced by tumor with only here and there gland yet lined by normal epithelium (Fig. 7). The tumor is papillary type with long, narrow branching stalks and secondary delicate streams. The cells vary frequently being irregular and poly while elsewhere there are tumor cells almost indistinguishable from the normal cells, differing only in having larger and paler nuclei, in more dense cytoplasm lacking the mucous globules. The neoplasia is interpreted as papillary adenocarcinoma primary in the ampulla of Vater which has extended onto the duodenal surface about the summit and into the common bile duct and pancreatic duct, and has infiltrated the fibro-muscular tissue of the duodenal wall. It has destroyed the normal structures of this region and has obstructed the ducts. Growth, as judged by the number of mitoses seen, has been quite active. Definite metastatic invasion is not demonstrated though slough of this tumor to adjacent tissue is well shown.

#### INCIDENCE OF CARCINOMA IN PERIAMPULLARY REGION

Should one rely only upon the number of cases in which surgical extirpation of a malignant lesion in the periampullary region has been done he would be inclined to the opinion that malignant disease in this situation is exceedingly uncommon. In 1927 Cohen and Colp collected from the literature only 59 cases of radical operation for carcinoma in the periampullary region of the duodenum, from 1868 to 1925 and these included 3 cases which they added. It has been possible for me to collect only 18 additional cases of radical extirpation for carcinoma of the ampulla of Vater since 1925 (including the case herein reported). The reported cases of radical extirpation of the ampulla of Vater fail to present a true idea of the incidence of malignant disease in this situation. Many more cases are recorded in which the lesion was found either to be inoperable at surgical exploration or was found at autopsy.

In 1913 Osterlind collected 10 cases of carcinoma of the ampulla of Vater. In only 2 of these had a resection of the ampulla been done. No attempt has been made in this review to collect all of the cases of carcinoma in the periampullary region of the duodenum that have been recorded. However search for the cases in which

radical operation has been performed has provided an opportunity for reviewing many cases in which palliative operations have been done for definitely determined malignant disease of the ampulla, or where the lesion was found at autopsy, to leave me with the impression that the cases in which radical operation was performed most conservatively represent less than 20 per cent of the cases of carcinoma in the periampullary region.

Upcott, Pallin, Einhorn and Stetten, Muller, Cohen and Colp, Busch, Fulde and others have previously presented extensive reviews of this subject. The report of Cohen and Colp provides a most complete collection of cases of radical operation for carcinoma of the ampulla in which 59 cases are listed since the first radical operation was performed by Halsted in 1898. The case reported by Abell has been deducted from Cohen and Colp's list, for it was not a radical operation for removal of the lesion, but was a case in which certain short circuiting operations were performed, and at a third and final operation transduodenal application of radium to the lesion was made. Considerable discrepancy is apparent in the collected cases published subsequent to those of Cohen and Colp. In 1927, Fulde collected 51 cases of radical operation, to which he added one of his own. He omitted 16 cases from Cohen and Colp's report (Alglave, Anschutz, Olami, Bruett, Gohrbrandt, Muller, Tenani, Della Valle, Pozzi, 3 cases, Cohen and Colp, 3 cases, Hartman, 2 cases, also reported by Stakevitch) and added 9 not previously recorded (Brenner, Boehm, Blad, Eiselberg, 2 cases, Konjetzny, Kappis, Wrede, Fulde). Of the latter it has been possible for me to verify only those of Konjetzny and Fulde. In 1931, Muller and Rodemaker stated that 81 cases were reported in the literature. However, an analysis of this report shows the inclusion of several cases in which radical extirpation was not carried out but in which the surgical procedure consisted of a palliative short circuiting operation. In 1933, Lauwers stated there were at that time 64 cases of radical removal of a carcinoma of the ampulla of Vater recorded. Actually about 85 cases are recorded to date. Appended are the abstracts of 17 cases collected since 1925, which, with the above reported case, and in conjunction with 58 cases collected by Cohen and Colp, provide a series of 76 cases of radical resection for carcinoma in the periampullary region of the duodenum, on which this study is based. Seven of these cases are from the Mayo Clinic. Three are contained in the series collected by Cohen and Colp, 2 having been recorded by W. J. Mayo, and 1 by Renshaw, in 1922. The 4 others are ap-

pended (Judd, 2 cases, Walters, 1 case, and Pemberton, 1 case). Two cases reported by Muller and Rodemaker (Van Remyne, Van Ardenne), and 7 cases reported by Fulde (Brenner, Boehm, Blad, Eiselberg, 2 cases, Kappis, Wrede) have not been available to me.

According to Springer, periampullar carcinoma may originate in the lower end of the common bile duct, in the ampulla of Vater, the duct of Wirsung, or from the duodenal surface of the papilla of Vater. Springer quotes Rolleston in stating that one-third of all new-growths of the bile ducts arise in the lower or terminal portion of the common duct. Growths originating here are practically always carcinomas and usually progress along the course of the duct and outward into the duodenal wall, infiltrating the mucosa and finally ulcerating freely into the duodenum. Rolleston has said that carcinoma arising in the ampulla of Vater, as such, is rare. Hanot termed this lesion *cancer du pylore pancreaticobiliaire* in contradistinction to neoplasm arising from the duodenal surface of the papilla or from the bile duct. It occurs as a small papillary outgrowth from the inner folds of the mucous membrane lining the ampulla. Neoplasms in the duct of Wirsung are rare. The new-growths arising from the duodenal surface of the papilla of Vater are the most common periampullar tumors and according to Springer comprise about two-thirds of all duodenal carcinomas. Murgoci has stated that the site of origin of cancer in the periampullar area is sometimes difficult to ascertain even on microscopic examination, and that observers have not all been careful to differentiate them. Practically all malignant lesions occurring in the periampullary region are carcinomas, most frequently adenocarcinoma or papillary carcinoma. Dencks, however, reported 2 cases of sarcoma, 1 of which was operated upon without success. Christopher reviewed 42 cases of benign tumor of the ampulla of Vater, 11 of which were papillomas. Case 1, that of Hansen, appended and included as carcinoma, reported as a benign papilloma at the time of excision with subsequent malignant recurrence, suggests that papilloma in this situation should be regarded as precancer if not actually malignant.

#### CLINICAL MANIFESTATIONS

There is nothing unusual in the age incidence of malignant disease in this situation for it corresponds with the age incidence of malignant disease elsewhere. It is of interest that the youngest patient in whom radical operation was done was 30 years of age, and that about 10 per cent of the

patients were in the fourth decade of life. The oldest patient operated upon was 66 years of age.

The clinical manifestations of malignant disease at the ampulla of Vater are those resulting from obstruction of the common bile duct and pancreatic duct, and from ulceration of the lesion with intestinal bleeding and secondary anemia. Jaundice has been a predominant clinical manifestation, intermittent or progressive with some pain associated in approximately 50 per cent of the cases, usually not as a true biliary colic unless gall stones were present. Outerbridge in a review of 110 cases of carcinoma in the perampullary area, found gall stones associated in only 30 per cent of the cases. While jaundice has been predominant, it has not always been present. Attention in several instances has been directed to indeterminate cause of intestinal bleeding, the source of which was found upon surgical exploration to be an ulcerating lesion of the ampulla of Vater. Diarrhea has occurred with sufficient frequency in the presence of pancreatic duct obstruction to be considered of significance, at any rate in the presence of jaundice. Denekhan, et al., in discussing 6 personal cases and 17 others collected from the French literature stated that in 11 cases there was intractable diarrhea. They emphasized the diagnostic significance of indeterminate intestinal bleeding and suggested that biliary obstruction, intestinal bleeding, and intractable diarrhea may give the clue to the diagnosis of ampullary cancer.

Seldom may the clinical diagnosis of perampullary carcinoma be made, and practically always the diagnosis has been established at the time of surgical exploration or at autopsy. The diagnostic difficulties of determining the cause of obstructive jaundice are well known. Judd has stated that too much significance should not be placed on the presenting symptoms in the differential diagnosis, for he has been led to believe that painless jaundice is commonly present in cases of obstruction from stone in the common duct, and furthermore that jaundice with colic and pain is more common in cases of carcinoma of the pancreas and ducts than was formerly believed.

The frequency with which carcinoma in the perampullary region of the duodenum, producing obstructive jaundice, has been found at autopsy as a locally confined, movable, and operable lesion without extension to surrounding structures and without metastasis, urges the adoption of the rather broad policy of exploring all cases of obstructive jaundice early in the absence of definite contra-indications. In applying such a general rule it will occasionally happen that through difficul-

ties of accurate differentiation an occasional case of non-obstructive jaundice, as proved upon exploration, will be operated upon. Such an occasional exploration is far less serious than to allow through the adoption of a more conservative attitude a case of obstructive jaundice caused by a surgically removable lesion to remain unexplored indefinitely.

Many have directed attention to the rapid decline of the patient with an obstructing perampullary lesion. Outerbridge stated that the average time elapsing between the onset of symptoms and death in 47 cases was 7½ months. In 50 per cent of the cases the duration was less than 3 months. The rapid decline of patients suffering from pancreatic secretion by way of an external pancreatic fistula or through pancreatic duct obstruction with pancreatic insufficiency occurring is well known. Abell has stated that cholelith and pancreatic insufficiency rapidly produce weight loss and anæmia.

#### SURGICAL PROCEDURES

So far as the operability of carcinoma of the perampullary region is concerned, the growth was limited to the papilla or its immediate surroundings, without glandular involvement or metastases, and surgically removable in three-fourths of the cases reviewed by Outerbridge. Such findings were repeatedly encountered at autopsy in the cases recorded during recent years. It is noteworthy that death usually takes place before metastases occur. Shapiro and Lifvendahl studied 18 cases of carcinoma of the extrahepatic bile ducts. Metastases were present at autopsy in all cases except the 1 case in which the lesion was situated in the ampulla of Vater. A feature common to nearly all these lesions is their small size. A common finding even at early operation when jaundice is present, or at autopsy is great distention of the gall bladder and common duct with colorless mucoid material entirely devoid of bile pigment.

Müller and Rodemaker have stated that the mortality rate of surgical procedures for carcinoma in the perampullary region ranges from 30 to 70 per cent, depending on the duration of the jaundice and the type of operation performed. From my review of the cases of carcinoma of the ampulla that have been operated upon, it may be stated that the mortality rate of palliative operations to provide internal biliary drainage by various types of anastomoses still approaches 70 per cent, while in recent years, through the employment of rather conservative methods of radical extirpation of the growth, the mortality rate of

TABLE I.—EIGHTEEN CASES OF RADICAL OPERATION FOR CARCINOMA OF THE PERI-AMPULLARY REGION OF THE DUODENUM FROM 1925-1934

Year	Surgeon	Operation performed	Result	Pathology
1922	Judd (Case 1) (Walters, 35)	1 Cholecystostomy 2 Transnodal excision choledochoduodenostomy	Died 2 days after operation	Carcinoma
1925	Hansen	Transduodenal excision cholecystostomy	Operative recovery recurrence and death 18 mos	1 Benign papilloma 2 Carcinoma
1925	Konjetzny	Combined transduodenal and retroduodenal excision Reimplantation C. D & P. D	Recovery	Adenocarcinoma
1925	Cabot (Potter)	Transduodenal excision Reimplantation C. D	Living and well 8 yrs after operation	Carcinoma
1927	Clar	Transnodal excision	Living and well more than 5 yrs after operation	Papillary carcinoma
1927	Fulde	Transduodenal excision	Living and well 2 yrs. after operation	Adenocarcinoma
1928	Coller (Potter)	Transnodal excision Reimplantation C. D	Died on fourth day (cholemia)	Carcinoma
1928	Busch	1 Cholecystostomy 2 Transnodal excision	Recovery	Adenocarcinoma
1928	Llambias	Transduodenal excision Reimplantation C. D & P. D cholecystec. & dr C. D	Recovery	Cylindrical cell epithelioma
1929	Dencks (Case 1)	Resection of duodenum. Reimplantation C. D to stomach	Died on the third day Autopsy No metastasis	Spindle-cell sarcoma
1929	Dencks (Case 2)	Transduodenal excision Reimplantation C. D & P. D Choledochostomy	Died on the sixth day postoperatively	?
1931	Walters	Transduodenal excision Choledochoduodenostomy	Recovery	Adenocarcinoma Grade II
1931	Pemberton (Walters)	Transduodenal excision C. D & duodenum Lateral anastomosis	Recurrence and death 2 yrs after operation	Colloid carcinoma
1931	Judd (Case 2) (Walters 34)	1 Drain gall bladder and common duct 2 Transduodenal excision	Recurrence 9 months after operation	Carcinoma
1933	Potter	Transnodal excision Reimplantation C. D & P. D	Recovery	Adenocarcinoma
1933	Lauwers (Case 1)	Transduodenal excision Cholecyst jejunostomy	Living and well 3 yrs. 10 mos. after operation	Cylindrical epithelioma
1933	Lauwers (Case 2)	Transduodenal excision. Cholecyst jejunostomy	Living and well 9 months after operation	Cylindrical epithelioma
1934	Hunt	Transduodenal excision. Reimplantation C. D & P. D Choledochostomy	Recovery	Adenocarcinoma

resection is decreasing and approaches 30 per cent. By rather conservative methods of radical extirpation I have reference to the direct reimplantation of the common and pancreatic ducts into the duodenum instead of extensive anastomoses between the gall bladder and stomach, duodenum, or jejunum to provide internal drainage of the biliary tract. The mortality rate is materially influenced by the magnitude of the surgical procedure. Radical extirpation has been facilitated as a second stage operation in a number of instances after preliminary external drainage of the biliary tract has been established as was first successfully accomplished by W. J. Mayo. The mortality rate in general of radical extirpation of a carcinoma of the ampulla has exceeded 40 per cent. In Fulde's collected series of 52 cases of radical operation, the mortality rate was 42 per cent. In 58 cases reported by Cohen and Colp there were 25 surgical

deaths, a mortality rate of 43 per cent. Of the 18 cases herein added to Cohen's and Colp's, there were but 4 surgical deaths, or a total of 29 in 76 cases, a mortality of 38 per cent for entire series.

The cases of radical extirpation herein considered were all operated upon as a one stage operation, with the exception of 8 cases, with only 2 deaths resulting from the second stage resection of the growth. This should not lead to the conclusion that the mortality rate of the two stage operation is more favorable than that of the one stage procedure, for the risk of establishing external biliary drainage or internal drainage by some type of anastomosis between the gall bladder and upper gastro-intestinal tract in the presence of obstructive jaundice is not negligible, by any means, and many patients who have been subjected to such preliminary procedures have not survived to undergo radical excision of the growth.

TABLE II—SURGICAL PROCEDURES IN SEVENTY-SIX RADICAL OPERATIONS FOR CARCINOMA AT THE AMPULLA OF VATER

(54 Cases of Colon and Culp and 22 bertha collected)

Operation	Cure	Deaths	Per cent
Transduodenal excision	69	14	20
Transduodenal excision only		70	41
Transduodenal excision with reimplantation C. D. or C. D. & P. D.		79	71
Transduodenal excision with reimplantation C. D. or C. D. & P. D. with internal or external drainage		3	41
Transduodenal excision without reimplantation C. D. or P. D. with internal or external drainage		6	6
Resection duodenum			21
Retroduodenal excision			70
	70	79	21

Tables I and II indicate several interesting factors pertaining to mortality rate. Transduodenal excision has been the most frequent method of extirpation of the growth in the perampullary region of the duodenum. Simple transduodenal excision without regard to some disposition of the common and pancreatic ducts apparently is accompanied by approximately the same risk as the more formidable procedures which in addition to excision of the growth include cholecystectomy or choledochostomy for external drainage or the various types of anastomoses or side tracking operations to provide internal drainage. In some instances, the operations have been of such magnitude as to include resection of a part of the pancreas, cholecystectomy and provisions for both internal and external drainage of the biliary tract. Transduodenal excision of the lesion with reimplantation of the common and pancreatic ducts into the posterior wall of the duodenum has apparently been carried out with the least possible risk.

Palliative operations whereby biliary obstruction is relieved by some anastomotic procedure between the gall bladder and upper gastrointestinal tract, even though executed with considerable risk, are often productive of much palliation though life may be prolonged for a matter of only a few months. Lauwers states that an anastomosis between the gall bladder and the jejunum obviates much more certainly the development of cholangitis, than where such anastomosis is made to the stomach or duodenum. In 1913, Erdman reported most excellent palliation derived from cholecystojejunostomy for carcinoma of the ampulla of Vater. Hingst's patient lived 5 years following a palliative cholecystoduodenostomy

Recurrence following radical extirpation of periampullar carcinoma has been frequent. Ten of the 47 cases that survived the operation lived less than 1 year, and in a number of other recurrences required subsequent operation for recurring jaundice or duodenal obstruction. Muller and Rodemaker's patient, despite the need of three operative procedures, lived 4 years in comparative comfort. Clar reported his case as the fourth one recorded living 5 years or more. He included those of Koerte, 17 years, Lewis, 8½ years and Oehler 6 years. Muller and Rodemaker stated that Koerte's case was living and well 22 years after operation. Among additional patients living 2 to 8 years after operation are those of Finkle, Cabot, Lauwers, Oltani, Thurn, Morin, and Novarro.

#### ABSTRACT OF SEVENTEEN CASE REPORTS OF RADICAL RESECTION OF CARCINOMA OF THE AMPULLA OF VATER, COLLECTED SINCE 1925

JURO (personal communication, Walters, 31) The patient was a man, 55 years of age, whose complaint was upper abdominal distress of 4 months' duration, and jaundice for months. Upon examination, the gall bladder was palpable, the patient was deeply jaundiced, the temperature was 101 degrees F and the leucocyte count as 7,000. At exploration, December 27, 1921, the liver was enlarged and the gall bladder and the common duct were distended. A hard, irregular nodule was felt. (The lower end of the common duct which was thought to be carcinoma of the ampulla of Vater.) A cholecystectomy was done to relieve the biliary obstruction with the idea of exposing the tumor of the ampulla of Vater. A second stage operation. The gall bladder contained dark bile. The convalescence from this operation as satisfactory and the patient subsided and the patient gained in weight and strength. On March 24, 1922, transduodenal resection of the ampulla of Vater was done, also choledochoduodenostomy. The patient died March 26, 1922, days after the operation. Autopsy revealed extensive hemorrhage into the gastro-intestinal tract and into the peritoneal cavity marked trophy of the liver, and diffuse hepatitis.



Fig. 1 Tumor of ampulla of Vater visualized upon opening duodenum.

HANSEN, 1925 The patient was a man 44 years of age, who was first seen June 6, 1924. The complaint was that of jaundice, fever, vomiting of coffee ground like material, and loss of 10 kilograms in weight. The liver edge was palpable just below the costal margin and a distended gall bladder was palpable. There was bile in the urine and some blood in the stool. The pre operative diagnosis was cancer of the pancreas, cholangitis, and probable ulcer of the duodenum near the papilla of Vater. At operation, August 15, 1924 the gall bladder was distended with colorless mucoid material, but contained no stones. There was some enlargement of the liver, but no abscess or metastases in the liver. On palpation of the duodenum a tumor was felt in the second portion, which was thought to be a tumor of the papilla of Vater. A transduodenal excision of a pigeon's-egg sized tumor was made without excision of the entire thickness of the posterior wall of the duodenum. The cut end of the common duct was seen and only a few sutures were introduced between it and the duodenal mucosa. A cholecystostomy was done. The patient made a satisfactory recovery and healing of the wound occurred without a

fistula. The pathological report was benign papilloma of the papilla of Vater.

Subsequent course The patient continued to improve for a time and regained the lost weight. Occult blood appeared in the stool and the hemoglobin dropped to 42 per cent. At the second operation, December 3, 1924 (6 months after the first operation), recurrence of the tumor at the head of the pancreas and metastases to the liver were found. A specimen removed proved to be carcinoma. The patient died 1 year later. Note This case is included for the final diagnosis was carcinoma, even though the original report on the tumor removed was benign papilloma.

KONJETZNY, 1925 The patient was a man, 55 years of age. The history was that of cramp like pain in epigastrium and jaundice of 6 weeks' duration. The gall bladder was palpable. The diagnosis of tumor of the papilla of Vater or of the head of the pancreas was made. At operation a tumor of the ampulla of Vater was found. The duodenum was mobilized and retroduodenal division of the common duct and the pancreatic duct with resection of segment of the head of the pancreas was accomplished. A

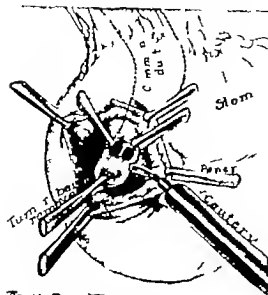


Fig 3 Method employed in excision of tumor

transduodenal resection of the tumor was made and the common duct and pancreatic duct were resected into the posterior wall of the duodenum. A small tube was inserted into the pancreatic duct. The patient made satisfactory recovery. The pathological report was adenocarcinoma.

CASE 7 (reported by Potter) is 915. Cabot made transduodenal resection of the lower end of the common

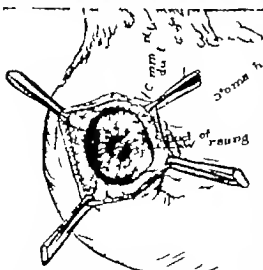


Fig 4 Common and pancreatic ducts resected into posterior wall of the duodenum

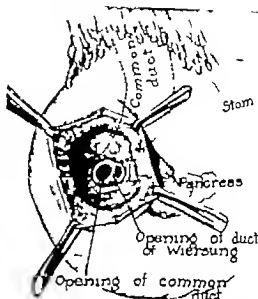


Fig 5 Dilated common and pancreatic ducts vascularized after excision of tumor

duct for robin's-egg sized carcinoma, in 1907 was 35 years of age. The carcinoma duct was resected into the duodenum. Four years later cholecystectomy was done for empyema of the gall bladder at which time the tube extending from the common duct into the duodenum was still present. In 1931 8 years after the original operation, the patient was in good health without recurrence of jaundice. Pathology carcinoma of the ampulla of Vater.

CASE 8, 1917, 927 The patient was male, 50 years of age. The history was that of epigastric pain and jaundice of 5 months' duration. On physical examination the gall bladder was palpable. The pre-operative diagnosis was carcinoma of the biliary ducts. Operation, January 1, 1917. There was large dilatation of the gall bladder and the common duct, both of which contained white bile. The biliary obstruction was found to be due to a tumor at the ampulla of Vater. A transduodenal excision of the tumor of the papilla with excision of 10 millimeters of the common duct and 5 millimeters of the pancreatic duct was made. Pathology papillary carcinoma. Subsequent course 4 weeks after operation the jaundice had entirely disappeared. March 2, 1917 (more than 5 years after operation), the patient was perfectly well.

CASE 9, 1917 The patient was male, 45 years of age. The history was that of painless jaundice of 5 months' duration. On physical examination large gall bladder was palpable. A pre-operative diagnosis of carcinoma of the liver or of the common duct was made. At operation large distended gall bladder was found and the common duct was dilated to the size of the little finger. A tumor at the ampulla of Vater was found producing complete occlusion of the common duct. Transduodenal excision of the tumor of the ampulla was made. Pathology adenocarcinoma. Subsequent course the patient was living and well 7 years after operation.

CASE 10 (reported by Potter) did transduodenal resection in 1923, similar to that in Cabot case, of the common

duct in a 64 year old man. Death occurred on the fourth postoperative day from cholemia and inanition. Pathology carcinoma.

BISCH, 1928. The patient was a man, 54 years of age. The history was that of repeated attacks of epigastric pain referred to the right shoulder, followed by jaundice. At a first operation a cholecystostomy was done without recognition of the cause of the obstructive jaundice. Postoperative recurrent colic and jaundice led to a diagnosis of hepatitis and cholelithiasis. At the second operation by Professor Schaldenose, a tumor of the ampulla of Vater was found and a transduodenal excision of the tumor was made. Recovery occurred. Pathology adenocarcinoma.

LEAMING, 1928. The patient was a man, 42 years of age. The history was that of epigastric pain of 1 year's duration, occurring several hours after meals. There had also been some nausea and vomiting of acid like material. The stools had also on several occasions been dark. No statement was made regarding the presence of jaundice. A clinical diagnosis of gastric ulcer or cholecystitis was made. At operation, July 30, 1927, no ulcer was found, however palpation through the anterior wall of the duodenum suggested a tumor of the second portion of the duodenum. The gall bladder, cystic and common ducts were greatly distended. A transduodenal excision of a tumor of the papilla of Vater was made and the common duct and pancreatic duct were reimplanted into the posterior wall of the duodenum. The gall bladder was removed and external drainage of the common duct was instituted. Recovery of the patient occurred. The pathological report was cylindrical cell epithelioma of the papilla of Vater.

DENCKS, Gustav, 1929 (Case 1.) The patient was a woman, 31 years of age, who entered the clinic January 25, 1923. The history was that of upper abdominal pain, jaundice, fever, loss of appetite and loss of weight of 2 months duration. The pain in the epigastrium was that of pressure. The patient was under observation for about 4 weeks at which time a pre-operative diagnosis of carcinoma of the duodenum or the pancreas was made. At operation, February 24, 1923, a small apple sized tumor was found in the region of the papilla. A resection of the duodenum including the tumor and a part of the pancreas was made with end to end anastomosis of the duodenum to the stomach and reimplantation of the end of the common duct into the pars pylorica. Pathology spindle cell sarcoma. Death occurred on the third day and at autopsy no metastases were found.

DENCKS, Gustav, 1929 (Case 3.) The patient, a man, was first seen October 18, 1926. On September 5, 1926 the urine was dark colored. The next day some upper abdominal pain and jaundice were first noticed. The symptoms persisted and on February 16, 1927, a pre-operative diagnosis of obstructive jaundice due to tumor was made. At operation, February 19, 1927, a large distended gall bladder was found which contained no stones, but did contain colorless or white bile. The common duct was sufficiently dilated to allow introduction of the finger after it was opened. A tumor at the ampulla the size of a walnut was found. Transduodenal excision of the tumor was made and the common and pancreatic ducts were reimplanted into the posterior wall of the duodenum and the common duct was drained externally. Pathology of the tumor was not stated. Death occurred on the sixth day and autopsy revealed no metastases.

WALTERS, Waltman, 1931. The patient was a man, 50 years of age, whose only symptom was severe intestinal bleeding. There had been no jaundice, but for 2 weeks there had been weakness, dizziness, and shortness of breath and a weight loss of 15 pounds. Indeterminate source of intestinal bleeding led to abdominal exploration,

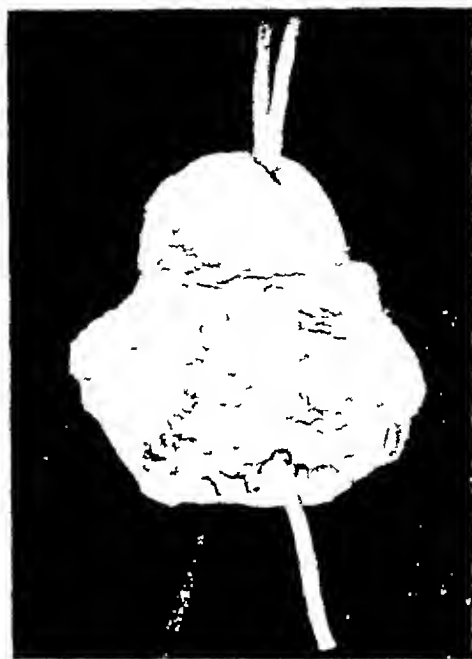


Fig 5 Lateral view of resected papilla. Catgut has been passed into the common bile duct and pancreatic duct and may be seen projecting through the meatus of the ampulla. Note the zone of smooth mucosa over the apex where there is neoplastic replacement of the epithelium.  $\times 4$ .

July 23, 1931. At operation palpation of the duodenum in the region of the ampulla revealed some thickening which in conjunction with distention of the gall bladder, could not be disregarded. The duodenum was opened and an ulcerating lesion approximately 2 centimeters in diameter, involving the ampulla and the posterior wall of the duodenum was revealed. Transduodenal resection of the entire thickness of the posterior wall of the duodenum, including the ampulla of Vater, beginning 1 centimeter beyond the periphery of the lesion and carried to the pancreas was accomplished, and the posterior wall of the duodenum was closed. No attempt was made to isolate or identify the pancreatic duct. The common bile duct was divided above the duodenum and the proximal end was anastomosed to the duodenum over a piece of catheter. The pathological report was adenocarcinoma, graded 2, of the ampulla of Vater. The convalescence was satisfactory and on re-examination of the patient 2 months later the general condition was excellent.

PEMBERTON (reported by Walters, 34). The patient was a man, 44 years of age, whose complaint was that of stomach trouble. Following careful clinical investigation the diagnosis was indeterminate and abdominal exploration was advised. At operation October 8, 1924, a markedly distended gall bladder was found. The appendix and gall bladder were removed. There were no gall stones. The patient returned 3 months later, January, 1925, with the history that 3 weeks previously pruritus had developed, and that this had been followed by gradually deepening jaundice without pain. At operation complete obstruction of the common bile duct, due to carcinoma of the ampulla, was found. The common duct was greatly dilated and con-





Fig. 6 Transverse section through papilla in horizontal plane (viewed from below). Note (1) normal duodenal mucosa on or the right and left folds, (2) neoplastic involvement of surface about the orifices, (3) nodules of tumor in papilla, all of right duodenal fold, (4) greatly dilated common duct (below left) and pancreatic duct (below on right), (5) walls and surfaces of terminal ducts and ampulla and replaced by papillary tumor tissue and normal passage ways occluded.  $\times 4$ .

turned whit. Sordid, mucous material. Transduodenal anastomosis by cautery of tumor of the papilla, 5 by 5 centimeters in diameter was made. Lateral anastomosis

as bridge between the common duct and the duodenum, and the cut end of the pancreatic duct was sutured to the duodenal mucosa. The pathological report was colloid carcinoma. The patient's general health remained good for months, when pain developed and jaundice recurred. Exploration September 30, 1926, disclosed extensive recurrence. Death occurred in March, 1927, little more than years after extirpation of the tumor of the ampulla.

Case (reported by Walters, 34). The patient was 30 years of age. Loss of weight and jaundice were present just before, of 3 1/2 months duration, and loss of 47 pounds. At operation, November 1925, the gall bladder and common duct were greatly dilated. A soft, movable tumor was found at the end of the common bile duct. Because of its tumor character and the prolonged coagulation time it seemed advisable only to establish drainage which was accomplished by cholecystostomy and cholecystostomy. One month later transduodenal resection of the ampulla of Vater was performed. Nine months later became of pain and recurring jaundice, abdominal exploration was carried out, which revealed structure or recurring carcinoma of the ampulla of Vater. Cholecystopneumostomy was performed. Seven months later palliative gastro-enterostomy was made.

POTTER, Eugene B. 213. The patient was woman, 57 years of age. The history was that of epigastric pain of 3 months duration and jaundice of weeks duration. The liver and distended gall bladder were palpable. A preoperative diagnosis of carcinoma of the head of the pancreas was made. At operation March 6, 1935, the gall blad-

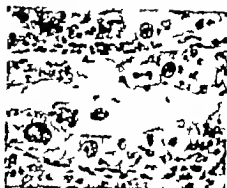


Fig. 7 Neoplastic replacement of epithelium in gland. The tumor cells are large, varying from cuboidal to columnar in shape usually by large nuclear nuclei and large prominent eosinophilic cytoplasm. Degeneration and necrosis are fairly prominent here. Normal cells show smaller and more dense nuclei and the cytoplasm usually contains numerous globules.  $\times 200$ .

der as thickened and about three times normal size and contained uncontracted bile. The cystic and common ducts were greatly dilated, but neither the gall bladder nor ducts contained stones. Palpation through the duodenum revealed movable, firm, hard mass, about 3.5 centimeters in diameter. The duodenum was opened and an incision was made involving the papilla was disclosed. The posterior wall of the duodenum with the tumor was lifted anteriorly and about 5 centimeters of the common duct was dissected free and transduodenal anastomosis of the tumor and end of common duct with cuff of duodenal mucous membrane 5 centimeter wide surrounding the anastomosis was made. The dilated common duct and pancreatic duct were then placed into the posterior wall of the duodenum. Ten small tubes were inserted into the common and pancreatic ducts. The patient made an unusual recovery. Final diagnosis adenocarcinoma.

LA WREN, 1933 (Case 3). The patient was man, 57 years of age. He was first seen in the Clinic September 4, 1920. The history of 4 months' duration, consisted of severe irritative jaundice and epigastric pain accompanied by constipation. At the time of examination the jaundice was very deep, the liver edge extended below the costal margin, but the gall bladder was not palpable. X-ray examination of the stomach was normal, however there was obstruction of the duodenal shadow. At the level of the ampulla of Vater. A diagnosis of tumor of the duodenum was made. At operation, September 24, the liver was somewhat enlarged. The gall bladder was not distended and did not contain stones. Palpation of the duodenum revealed firm mass. The duodenum was opened and transduodenal cavity extension of ulcerating strawberry sized tumor of the ampulla of Vater was made. A cholecystopneumostomy was made after the jejunum was divided, making the anastomosis between the gall bladder and distal end of the jejunum, replacing the proximal end of jejunum into the side of the distal jejunum. The confluence was satisfactory and the patient was discharged from the Clinic 3 weeks after the operation. The pathological report was cylindrical epithelioma. The patient was seen again July 4, 1933, 3 years and 10 months after operation at which time he was in good health.

LA WREN (Case 4). The patient was man 5 years of age, seen in the Clinic October 14, 1933. The symptoms

were vague epigastric pain and recent jaundice. The gall bladder was palpable. At operation October 18, 1932, the liver was considerably enlarged and the gall bladder was greatly distended but did not contain stones. Transduodenal excision of an ulcerating pea sized tumor of the ampulla of Vater was made, suturing the end of pancreatic duct to the duodenal mucosa. The common duct was dilated and a cholecystojejunostomy was made between the distal jejunum, after its division, and the gall bladder, and the proximal end of the jejunum was implanted into the distal jejunum. The pathological report was cylindrical epithelioma. The convalescence was uneventful and the patient was dismissed 17 days after operation. Nine months later, the patient was perfectly well.

The following cases have not been available for review: Brenner, Boehm, Blad, Eiselberg (2 cases), Kappis, Wrede (reported by Fulde), Van Remyne, Van Ardenne (reported by Muller and Rodemaker).

## REFERENCES

- 1 ABELL, IRWIN. Carcinoma of the papilla of Vater. *South. M. J.*, 1924, 17: 24-27.
- 2 BUSCH, E. Et Tilfaelde af Operativt Behandlet Carcinoma Papillae Vateri. *Hosp.-Tid.*, 1928, 71: 1415-1420.
- 3 CABOT. Quoted by Potter.
- 4 CHRISTOPHER, FREDERICK. Adenoma of the ampulla of Vater. *Surg., Gynec. & Obst.*, 1933, 56: 202-204.
- 5 CLAR, FRITZ. Karzinom der Papilla Vateri, excision, Heilung ueber 5 Jahre. *Zentralbl. f. Chir.*, 1927, 54: 2119-2120.
- 6 COHEN, IRA, and COLP, RALPH. Cancer of the periampullary region of the duodenum. *Surg., Gynec. & Obst.*, 1927, 45: 332-346.
- 7 COLLIER. Quoted by Potter.
- 8 DENCKS, GUSTAV. Beitrag zur Diagnose und operativen Behandlung maligner Tumoren der Papilla Vateri und des Pankreas Kopfes. *Deutsche Ztschr. f. Chir.*, 1929, 213: 147-158.
- 9 DENECHAU, D., TANGUY, A., and VERANGOT, P. Le Cancer de l'ampoule de Vater. *Bull. méd.*, 1931, 45: 535.
- 10 EINHORN, M. and STETTES, DEW. Carcinoma of the ampulla of Vater. *Med. J. & Rec.*, 1924, 120: 101-106.
- 11 ERDMAN, J. F. Carcinoma of the papilla of Vater. *Ann. Surg.*, 1913, 58: 687-688.
- 12 FULDE, EWALD. Die bekantsit gewordenen Ergebnisse der Radikaloperationen der gallengangskrebse. *Zentralbl. f. Chir.*, 1927, 54: 1481-1487.
- 13 HALSTED, W. B. Contributions to the surgery of the bile passages especially the common bile duct. *Johns Hopkins Hosp. Bull.*, 1899, 141: 645-654.
- 14 HANSEN, AF SVEND. Et operativt Behandlet Tilfaelde af Perampullaer Duodenalkarsinom. *Ugesk. f. Læger*, 1925, 35: 755-756.
- 15 HINGST, J. W. Een geval Van Kanker van de Papilla Vateri. *Nederl. Tijdschr. v. Geneesk.*, Haarlem, 1926, 70 Pt. 2, 1769-1775.
- 16 JUDD, E. S. "Side tracking" operations in obstructive jaundice. *J. Am. M. Ass.*, 1928, 16: 300-304.
- 17 KOVJETZKY. Radikale Operation eines Carcinoms de Papilla Vateri (einzeitige transduodenale Resektion). *Klin. Wchnschr.*, 1925, 4: 426-427.
- 18 LAUWERS, E. Traitement chirurgical du cancer Vaterien. *J. de chir.*, 1933, 42: 833-842.
- 19 LEWIS, R. M. Cancer of the ampulla of Vater. *Surg., Gynec. & Obst.*, 1921, 32: 545-545.
- 20 LLAMBIAS, J., BRACHETTO-BRIAN, D., and OROSCO, G. Contribucion al estudio de cancer de la ampulla de Vater. *Semana med.*, 1928, 2: 649-666.
- 21 MARSHALL, JAMES M. Tumors of the bile ducts. *Surg., Gynec. & Obst.*, 1932, 54: 6-12.
- 22 MAYO, W. J. Cancer of the common bile duct. Report of a case of carcinoma of the duodenal end of the common duct with successful excision. *St. Paul M. J.*, 1901, 3: 374-380, Collected Papers Mayo Clinic, 1912, 1: 364-371.
- 23 MULLER, G. P. Carcinoma ampulla of Vater. *Tr. Am. Surg. Ass.*, 1925, 43: 393-400.
- 24 MULLER, GEORGE P., and RODEMAKER, LEE. End results in radical operations for carcinoma of the perampullary region of the duodenum. *Ann. Surg.*, 1931, 93: 755-760.
- 25 MURGOCI, HELEN B. Six cases of cancer arising in tissues within the duodenal loop. *Bristol M.-Chir. J.*, 1927, 44: 195-208.
- 26 OUTERBRIDGE, G. W. Carcinoma of the papilla of Vater. *Ann. Surg.*, 1913, 57: 402-426.
- 27 PALLIN, G. Des Carcinom des Ductus hepaticocholedochus und seine chirurgische Behandlung (52 Schwedische Faelle). *Beitr. z. klin. Chir.*, 1920-1921, 121: 84-137.
- 28 POTTER, EUGENE B. Successful resection of the common biliary duct for carcinoma of the ampulla of Vater. *Ann. Surg.*, 1933, 68: 369-373.
- 29 RENSCHAW, K. Malignant neoplasms of the extrahepatic biliary ducts. *Ann. Surg.*, 1922, 76: 205-221.
- 30 SHAPIRO, PHILIP F., and LIFVENDAHN, RICHARD A. Tumors of the extrahepatic bile ducts. *Ann. Surg.*, 1931, 94: 61-79.
- 31 SPRINGER, EARNEST. New growths involving the terminal bile and pancreatic ducts. *Boston M. & S. J.*, 1925, 192: 997-1000.
- 32 STAKEVITCH, V. Contribution à l'étude des neoplasmes de l'ampoule de Vater. *Paris*, 1914.
- 33 URCOTT, H. Tumors of the ampulla of Vater. *Ann. Surg.*, 1912, 56: 710-725.
- 34 WALTERS, WALTERMAN. Successful resection of the ampulla of Vater, including a portion of the duodenum with choledochoduodenostomy for carcinoma of the ampulla of Vater. *Surg., Gynec. & Obst.*, 1932, 55: 648-651.
- 35 Idem. Personal communication.

# COMPLETE EXCISION AND RECONSTRUCTION OF BOTH ACHILLES TENDONS FOR GIANT CELL XANTHOMA

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IT is not now an everyday occurrence for the surgeon to be confronted with a situation in which there is no precedent, either in the literature or in his own experience upon which to base a plan of action. The case reported below is such a one. Tumors of tendons are so rare that some writers even doubt their existence (Burton) we can find only one instance in which an Achilles tendon has been excised and a transplant of fascia lata made. In this case (McWhorter and Weeks) there is no mention of the end-result so that we do not know whether or not function was regained. The outcome of treatment in our patient seems to me to be of more than passing interest.

**MRS. SMITH** No good Patient, 40, white, married woman, aged 40 years. She first entered Strong Memorial Hospital out-patient department August 31, 33, with complaint of morning nausea and vomiting. She was followed for a period of 5 months in the medical and gynecological clinics. The diagnoses as that the cause of the morning nausea and vomiting was most likely psychic. This opinion was based on the fact that the patient wanted a child and had never become pregnant. She was admitted to the hospital on November 18, 33, and dilatation, curettage, and Ruben's test carried out, no cause for the sickness was found, except that the uterus was inflexible in type.

During this period the patient had no complaints referable to her Achilles tendons, and numerous examinations by different observers showed the lower extremities to be normal. She was discharged on December 4, 33.

Two weeks following discharge she returned to the gynecological clinic complaining for the first time of low back ache with pain radiating down the posterior aspect of both thighs into the calves. She was referred to the orthopedic clinic here, saw her for the first time on January 27, 34.

The impression at this time was that she had low back strain. X-ray films of the sacro-lumbar joints and lower lumbar spine showed no pathological changes. She was treated with baking and massage to the back and firm bed at home. Under this regimen the backache improved somewhat.

On February 24, 34, she complained for the first time of pain in both Achilles tendons. Examination showed that there was thickening of both tendons with pain on dorsiflexion of the feet to 90 degrees, more marked on the left. She was treated by strapping both ankles to hold the feet in moderate plantar flexion and elevating the heels one-fourth inch. This as continued over a period of months but afforded the patient no relief. In fact, the swelling of the tendons and the tenderness on palpation seemed to increase steadily. Her symptoms increased to such point that she was put to bed at home for a period of weeks and advised to apply external heat for a period of an hour three times a day. At the end of this time she was not improved. She now had so much pain in her heel cords on sitting that it was difficult for her to get around and she relied with shuffling gait, keeping her ankle joints

as nearly fixed as possible. She was advised to enter the hospital for exploration of the tendons with diagnosis of bilateral chronic tenosynovitis of the Achilles tendons.

She was admitted to the hospital for the second time on April 4, 1935. Complete present and past histories revealed nothing of significance except as already stated.

Physical examination showed fairly well developed, thin girl of 40 years, who appeared chronically ill. The skin was elastic, moist, with moderate amount of subcutaneous fat. There were no xanthomatous deposits. There was no lymphadenopathy. The head was normal. Hearing was roughly normal, with no abnormality of the external auditory canals or ear drums. The eyes and nose were normal. The mucosa of the mouth was of good color. The teeth were extremely carious. The tonsils were somewhat enlarged. There was moderate, diffuse, non-nodular enlargement of the thyroid. The chest and breasts presented no abnormalities. The lungs were clear and the heart was normal. Abdominal examination showed no masses or palpable nodes. Pelvic examination showed uterus to be of infantile type. Reflexes are in order throughout.

Both Achilles tendons were thickened to about twice their normal width. They were extremely tender to palpation and left rough and nodular. The involved area extended upward for about 5 centimeters from the os calcis in each tendon. Dorsiflexion of the feet was painful and voluntarily limited to about 90 degrees. The appearance of the Achilles tendons, showing their increased breadth and nodular character can be plainly seen in Figure 1 taken April 6, 1935.

Laboratory findings hemoglobin, 70 grams per 100 cubic centimeters, red blood cells, 4,400,000, late blood cells 6.5%. Urine was cloudy yellow, acid, specific gravity 1.020. No albumen or sugar. Microscopic examination showed an occasional epithelial cell. The Wassermann reaction was negative. Blood cholesterol (Woods' method) was 220 milligrams, average, on several determinations.

On the day following admission she began to complain of twinges of pain in both elbows, right shoulder and wrist. It was thought that this might be low grade infectious arthritis and that it and the tenosynovitis might have some relation to the infected teeth and large tonsils.

Accordingly the upper central and lateral incisors, which showed focal infection by X-ray were removed, and on April 24, 1935, tonsillectomy was carried out. This cleared no disturbance in the acrolydynamia whatever, although the joint symptoms disappeared.

On April 25, 1935, the left Achilles tendon was explored with the pre-operative diagnosis of chronic tenosynovitis with pain probably due to fibrous adhesions between the tendon and sheath. It was thought that freeing these might afford some relief.

Original operation Nitrogen oxide gas and ether anesthesia was used. The left lower leg was scrubbed with soap and water followed by alcohol and ether and then painted with two coats of methaphen. The limb was draped with sterile stockinette. An incision about 6 inches in length was made longitudinally and parallel to the lateral edge of the Achilles tendon from its insertion into the os calcis upward. The skin and subcutaneous tissues were divided and the edges of the wound fastened with Michel clips to the stockinette to exclude the skin from the operative field.



Fig 1 External appearance of Achilles tendons, April 6, 1933, showing the increase in width and irregular contour. The nodules are quite hard and tender.

The tendon and its sheath were exposed. The sheath of the tendon had numerous other yellow deposits in it. It was dissected free from the tendon which was found to be about three or four times normal size. It was irregular in contour and on palpation was nodular and hard. The tendon was incised longitudinally, as the fibers were separated, numerous hard lemon yellow nodules were seen interspersed between the tendinous fibers. This process extended from the os calcis up to within about an inch of the origin of the tendon from the muscle belly of the gastrocnemius. It was obvious that the whole process could not be removed without completely excising the tendon. It was thought that the patient's symptoms might be due to the irregularity and increase in size of the tendon. A long longitudinal wedge was removed from the tendon so that when the free edges were approximated, the tendon was approximately normal size. The subcutaneous tissues and skin were closed. Interrupted fine silk was used throughout for suture material. No immobilization was used (Fig 2).

Following this procedure, the patient experienced considerable relief from pain on the side operated upon. The wound healed *per primam* and by the time the sutures were removed on the seventh postoperative day, motion of the left ankle was free and practically painless. We were encouraged and as the patient was continuing to complain of pain in the right tendo achillis, we decided to explore it.

Two weeks following the first operation (May 3, 1933) the right side was explored, an identical condition found and the same procedure carried out.

At the end of 10 days the patient was up walking although she still had pain in both tendons. She was discharged from the hospital on May 15, 1933 to be followed closely as progress of the process was to be expected, although it was thought that this would probably be slow. Figures 3 and 4 show the microscopic appearance of the tumor. In the sections one can see the tendon fibers separated by areas of invasive fibrous tissue. The connective tissue fibers are young and associated with numerous mononuclear and giant cells. The tissue is fairly vascular and resembles chronic granulation tissue. Fat stains reveal many lipochrome granules in the tumor cells. A diagnosis of giant cell xanthoma of the tendon was made.

The patient was followed at frequent intervals. She was never completely free of pain in the tendons although it

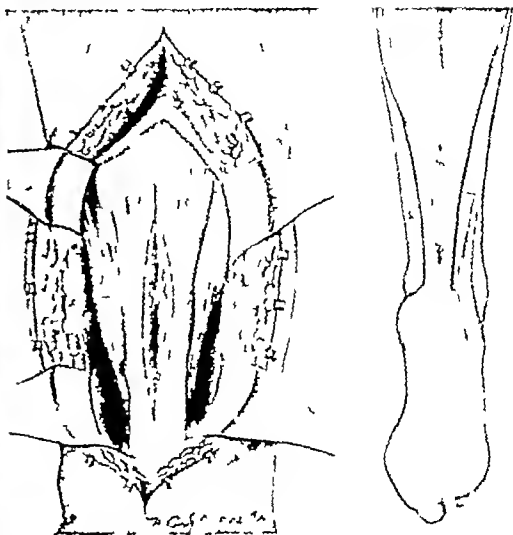


Fig 2 Drawing of operative findings and procedure carried out April 21, 1933. The tendon was three to four times normal size and irregular in contour. Hard, lemon yellow tumor nodules are scattered between the tendinous fibers. The condition is identical bilaterally. A wedge is removed longitudinally to reduce the size of the tendon and the edges resutured. Operations on April 21, 1933, and May 3, 1933.

first this was markedly decreased in severity. Deep X-ray therapy was started on July 19, 1933, and continued until September 15, 1933, when full course of therapy had been completed. A total of 2300 units was given in divided small doses.

At the end of this time there had been no relief in symptoms, on the other hand, the tenderness and pain had increased and she was able to walk only with difficulty. She was given a period of 3 weeks to secure maximum benefit from X-ray therapy but at the end of this time no relief was in evidence. It was decided that the only hope of cure was by complete extirpation of the tendons and reconstruction of them either by tendon transplantation or fascial lata.

She was admitted to the hospital again on October 17, 1933 about 5 months following original operations. The tendons at this time were again enlarged to about three times normal size by tender indurated nodules 1 to 2 centimeters in diameter. On the left, these extended 22 centimeters upward from the os calcis and on the right about 14 centimeters. Dorsiflexion was voluntarily limited at 110 degrees on both sides by pain in the tendons when they were stretched.

On October 18, 1933 under nitrous oxide gas and ether anesthesia after preparation with iodine and alcohol an incision was made along the dorsal lateral aspect of the right Achilles tendon from the os calcis to the upper third of the leg and the skin edges were clipped to sterile stockinette. There was extensive scarring in the region of the previous operation with firm adhesions about the tendons. The tendon was excised from its calcaneal insertion to within about 5 centimeters of the lower end of the gastrocnemius muscle. All indurated tissue was removed with a wide free margin proximally. A long longitudinal incision was made on the lateral aspect of the right thigh and a



Fig 3 Photomicrograph of the tumor tissue removed at first operation. A small area with giant cells is seen in the upper central portion of the section. Just below it are cells containing lipochrome granules, with special fat stains. These cells are quite numerous and are scattered throughout the tumor. The main mass of the tumor consists of relatively young fibroblasts replacing and invading the normal tendon structure which is seen running diagonally across the lower portion of the section.  $\times 40$



Fig 4 This shows the normal—dark staining—fibers of the tendon being invaded by an actively growing connective tissue.  $\times 40$

strip of fascia lata about 6 by 30 centimeters was removed. This was split 1 cm end to form three finger-like processes which were spread apart and secured separately into the spongerous over the resected end of the gastrocnemius. The distal end of the fascia was split into two processes and these were passed through drill hole in the os calcis and firmly sutured. The bone with braided silk sutures. The spinal nerve was preserved throughout the dissection. The wound was closed in layers with catgut and the skin with dermal. A plaster boot as applied with the foot in marked equinus to relieve tension on the reconstructed tendon, as it was not possible to secure a strip of fascia long enough to reconstitute the tendon with the foot in neutral position. The thigh wound was closed with catgut also. Figure 5 shows the excised tendon.

The postoperative course was uneventful. On October 23, 1934, 15 days following operation, she was discharged from the hospital on crutches. During convalescence the patient continued to have severe pain in the left lower extremity. The plaster boot was left on month. On removal, the wound was found to be well healed. There was about 40 degrees active flexion-extension in the ankle with manipulation about 55 degrees. The transplanted felt and functioned like normal Achilles tendon.

Massage, bulking, and exercises to overcome equinus and restore motion on the right side were begun. On November 29, 1934, operation was carried out on the left side. A exactly similar process was found; the entire tendon was excised and reconstruction was carried out in the same manner as described above. The ankle was immobilized in plaster boot with the foot in extreme equinus. The postoperative course was satisfactory.

The cast was removed at the end of 1 month and the wound found to be healed. Hydrotherapy, massage, and exercises were continued daily on each extremity. Progress in regaining motion and overcoming the equinus were of course slow.

On January 30, 1934, about 8 weeks following final operation, crutch walking with partial weight bearing was allowed. She was discharged from the hospital on March 3, 1934, able to walk for short distance without crutches. She returned every other day for continuation of physiotherapy. Her convalescence as retarded by an acute otitis media and mastoiditis which necessitated mastoidectomy on May 1934. Following recovery from this illness, her return to activity was quite rapid. On June 3, 1934, physiotherapy as discussed (approximately 5 months after reconstruction) as there is now normal range of motion in both ankle joints. At this time her main difficulty seemed to be one of maintaining equilibrium and learning to walk again.

During the next 3 months she gradually learned to walk. On July 4, 1934, about 8 months following reconstruction of tendons, she was walking quite well with only very slight limp. She was doing her own housework, had no pain in either tendo achilles region. Examination showed no evidence of recurrence of the tumor, although there was little tenderness and induration in the calcaneal insertion of the right tendon into the os calcis.

There was normal range of active motion in both ankle joints except for slight limitation of dorsal flexion and the reconstructed tendons functioned as normal mechanical units. There was still only fair power of plantar flexion. She was just barely able to support her weight on her legs but we have every reason to believe that this will rapidly respond with activity.

This patient, as one can see, presented a problem which theoretically was easy to solve but practically was had considerable tripping in the beginning about the eventual outcome. The procedures suggested themselves to us. The tendons evidently must be removed to relieve the patient but how should their function be re-established? We thought of transplanting the peroneal tendons into the os calcis and arthrodesing the midtarsal and subtarsal joints to compensate for the

muscular imbalance of the foot resulting from removal of the peroneals from the lateral side of the foot. This is commonly done in gastrocnemius palsy resulting from infantile paralysis. It provides a fairly good walking foot but the peroneals never furnish the power that the gastrocnemius-soleus group has. As long as the muscle seemed to be normal it would certainly be best and simplest to reconstitute the tendon. If this failed the peroneal transplantation could be used later.

Fascia lata has of course in recent years been used to reconstruct tendons and ligaments in many parts of the body, but could it be used to replace the largest tendon in the body and withstand the strain of lifting the whole body weight with each step? The only reference to such a use in the literature is in a case reported by McWhorter and Weeks in 1925. Their patient was a 39 year old negro who had "xanthoma tuberosum multiplex." The xanthomatous deposits involved not only the Achilles tendons but the patellar, triceps, and extensor tendons of the hand. To quote from their article "the mass from the region of the left tendo achillis was removed and a fascia transplant done. The specimen removed from the left ankle consisted of a large, circumscribed, encapsulated, and lobulated tumor mass, measuring 14 by 3.5 by 7 centimeters." There is no mention of follow-up on this patient or whether the tendon was a serviceable one.

In the original operations on this woman in which the tendons were pared down to somewhere near normal size, we again had no previous experience to guide us. But we later found an almost identical procedure had been reported by Ollershaw in 1923. His patient was an 18 year old girl who had hard, well defined tumors over both Achilles tendons about 2 inches above their insertions. The tumors were symmetrical and had grown slowly in size for about 3 years. She also had patches of xanthelasma on the skin of the right arm. He describes the operation as follows: "The tendon was very greatly thickened and had many yellow colored areas on its surface and also infiltrating its fibers. Certain of these patches were also present in the subcutaneous tissue. The tendon was trimmed down to a little more than its accustomed size and the skin repaired." Unlike our patient, there was no evidence of recurrence 3 years later. The microscopical sections in this case showed the typical giant and xanthoma cells.

As one can readily see these two reports while describing cases seemingly very similar to our case actually probably belong to an entirely different disease, namely, "xanthoma tuberosum multiplex." McWhorter's and Weeks' patient cer-



Fig 5 The excised tendons. The specimen on the left, even in the photograph, conveys the impression of the hard, nodular character of the tumor. Notice the great size of the tendon which normally is a thin ribbon about one half inch in width. Operations in October and November, 1933.

tainly does as the blood cholesterol by Bloor's method was 600 milligrams per 100 cubic centimeters. There are no blood cholesterol determinations reported by Ollershaw but the presence of xanthelasma almost surely places it in this group. If one considers the deposits in the skin and elsewhere in this systemic affection as true neoplasms, then there are a number of tumors of the Achilles tendons reported because they are one of the most common sites which the disease affects.

There has been a great deal written about "xanthoma tuberosum multiplex," the bulk of it in dermatological publications. It has been recognized as a somewhat rare clinical entity for many years. In 1882, Hutchinson tabulated 36 cases of multiple xanthoma, and in 1893, Torok reported and gave a résumé of 70 such cases. Both called attention to the fact that the manifestations of the disease were often present before puberty. Pinkus and Pick first called attention to the hypercholesterolemia practically always present in these patients. They remark that isolated xanthomas are probably true neoplasms and not associated with such a blood cholesterol increase.

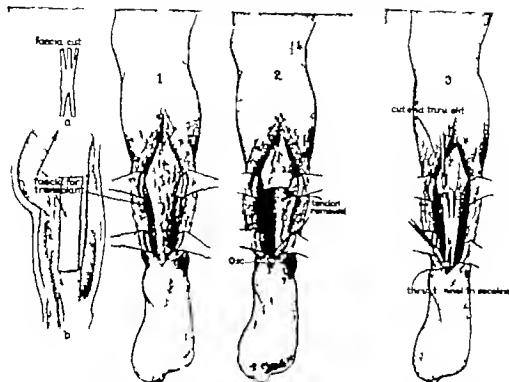


Fig. 6. Left, the tendon has been exposed through-out its entire length. The tumor extended completely down to the os calcis, but at the proximal end there was a small amount of healthy tendinous fibers to which the large fascial strap could be anchored.

Fig. 7. The method of making the transplant. The finger like processes of either end give strong attachment. The foot is in marked spasm for two reasons: enough length of fascia lata could not be obtained to bridge gap in neutral position, and to take strain off suture line.

Following the discovery of hypercholesterolemia, there have been articles supporting each side of the argument. Stewart divided the growths containing foamy cells into those in which there is an elevated blood cholesterol and those without such an increase. Levy expressed the same opinion. Beeson and Albrecht reported a case with the typical distribution of the tumors over the elbows, knees, heel cords, and thumb with increased blood cholesterol. They conclude from the literature that there is generally hypercholesterolemia in the disease. Silberberg maintains that even if it is true that imbalance of lipid metabolism may cause a secondary xanthelasma, there are xanthomatous tumors without metabolic disturbance. Harbitz takes the half way position. He calls attention to the fact that, in both multiple and isolated xanthomas, the tumors are located near tendons, and he believes that one cannot entirely reject the idea that the cholesterol seen in some of the isolated tumors is due to

hypercholesterolemia. There is, however a case reported of "xanthoma multiplex" in which there were no abnormal blood cholesterol values (Rosenthal and Braunisch).

On the other hand there are those who believe that all forms of xanthoma are associated with blood cholesterol values above the normal (Weber McWhorter and Weeks).

From a perusal of the material written on this subject, the conclusion is almost forced on one that there are two groups of tumors which can be easily separated clinically but which, microscopically, may be indistinguishable. Both may contain giant cells, xanthoma cells, cholesterol and actively growing connective tissue or any combination of these. Clinically there is the typical picture of "xanthoma tuberosum multiplex." In this condition there are other yellow patches in the skin such as one commonly seen in the skin of the eyelids. The tumors are multiple and have a predilection for areas subjected to



Fig 8 The patient on September 22, 1934, approximately 1 year after operation. There is no gross evidence of recurrence as yet, although there is some tenderness and slight induration at the insertion of the right tendon into the os calcis. In the bare feet there is still slight equinus evident. In shoes this is compensated for so that the gait is practically normal. The power in the gastrocnemii is shown by the ability to support the body weight on the toes.

trauma such as the extensor surfaces of the elbows, knees, hands, and feet and are often associated with tendons, especially the Achilles tendons and the extensor tendons of the hands. The tumors do not cause any symptoms until they become so large that they mechanically interfere with function. There is practically always an increase in the blood cholesterol.

The isolated giant-cell xanthomatic tumors also present a fairly typical clinical picture. They appear as small, slowly growing, benign swellings. Trauma seems to be an important factor in the etiology. They occur most frequently on the extensor surfaces of the hands and most commonly on the index finger of the right hand (Mason and Woolston, from records of 144 cases in literature). To a lesser extent, they are seen on the dorsum of the foot and about the ankle. They practically always arise from the tendon sheaths. There is no hypercholesterolemia. Our patient belongs in this group, although there is no question that the tumor was primarily one involving the tendon itself and not the sheath, which is quite rare.

There has been a great deal written about these giant celled xanthomas of tendon sheaths since Broca reported the first case in 1860. The early literature, most of it in French, is well covered in two reviews, the first by Heurtaux in 1891 and the more recent one by Tourneux in 1913. The latter, in an extensive review, collected 93 cases of tendon sheath tumors, about 54 of these should be classed as giant celled xanthomas. Among these cases only 8 were on the lower extremities and none of these was in connection with the Achilles tendon.

The nomenclature which has been used to describe the tumors is interesting. At first they

were referred to as sarcomas. But as clinical evidence accumulated, it was seen that they were essentially a benign process, even though Krogus, as late as 1922, thought that the benign view should be abandoned except for those tumors occurring on the fingers. Dor first described the xanthoma cells present in the growths and suggested the name myeloxanthoma. The English writers still refer to the tumors as giant cell myeloma or myelosarcoma.

In recent years, there have been two authors (King, 1931, and Morton of this clinic, 1934) who have suggested that the tumors of tendon sheaths probably all arise from synovial cells and would best be classified under a name suggesting this origin. King suggested the group name tenosynovioma with descriptive terms following, such as fibrous, cartilaginous, etc. Morton proposed the group of "synovigenic tumors" to include all tumors having their origin in the synovial membranes of tendons, bursae, joint capsules, and joint linings. Under this heading, he would place the giant cell xanthoma as one of the tumors which arises from tendon sheaths. It certainly seems that the term giant cell xanthoma is the one now in most common use and probably best describes the most common of all the tumors affecting the tendons and their sheaths.

At present the main argument concerning the giant cell xanthomas is concerning whether they are neoplastic or inflammatory in nature. As noted, almost everyone who has given any thought to the subject now agrees that the isolated tumors are not associated with a systemic derangement of lipid metabolism and that clinically they are benign and as such should be removed locally without recourse to extensive or mutilating opera-



bloes. But as to whether they are neoplasms or inflammatory reactions to local irritation, there is no general agreement.

Dor was probably the first to suggest that the tumors might be inflammatory in origin. The majority of writers before him assumed that the growth was sarcomatous, a view which is certainly not tenable at present. His views seem to be gaining ground and such writers as Flesberg, Broders, Janik, Arzt, Seyler, Kusnetzowky and Mason agree that the growths may well be only chronic inflammatory reactions to various irritants. Fleiszig and Seyler suggest that they be called granulomas of tendon sheaths. The other viewpoint held by many writers and originally advanced by Bellamy is that the growths are endotheliomatous in nature. He applied the term myeloid endothelioma to them and his followers include Beekman, Ragins, Stewart, Gonzalez Aguilar and others.

Whatever the nature of the underlying process be from a practical standpoint the important fact is that the tumors are benign, and treatment as in other types of benign growths, should consist of local eradication or excision. Recurrence is not an indication for amputation, but local eradication should again be carried out. In general these giant cell xanthomas should be treated in the same fashion as giant cell tumors of bone. Cases are reported in which the tumor has been removed three times before cure was effected and amputation thus avoided.

In most cases the tumor can be easily removed without the necessity of sacrificing the tendon as it is very rarely involved. But if it should be necessary to excise an important tendon our experience indicates that fascia lata may be transplanted, will persist and will bear as great strain as any tendon would need to undergo.

#### SUMMARY

Tumors of tendons are very rare. A case of isolated giant cell xanthoma tumor affecting both Achilles tendons is reported. There was no hypercholesterolemia which excludes the patient from belonging to the group of xanthoma tuberosum multiplex. Both Achilles tendons were completely excised and new tendons reconstructed with fascia lata. Eight months following operation the reconstructed tendons are functioning as normal mechanical units.

#### BIBLIOGRAPHY

VERMIGLI, M. Contributo allo studio dei tumori delle guaine tendinee. *Ann ital di chir* 925 7 20-43

- ARTZ, L. Beiträge zur Xanthom (Xanthomatose) Frage (C) Pseudonanthomatose Bisheriges. *Arch f Dermat u Syph* 810, 25 609-93
- BECKEN, A. F. Giant-cell tumors of the tendon sheaths. *Ann Surg* 915 6 737-743
- BELSON, B. B. and ALBRECHT, P. G. A contribution to the study of xanthoma tuberosum, with report of case. *Arch Dermat u Syph* 9 3 8 495-714
- BELLAMY, H. F. The myeloid tumor of tendon sheaths. *J Path & Bacteriol* 90 7 469-480
- BERTI, G. Contributo allo studio dei granulomi delle guaine tendinee. *Tumori* 9 3- 924, 20 460-47
- BONNARD, A. and CHENEY, A. Fibrome herve nappée (Sarcome myélopiaque des guaines tendineuses). *J de méd de Bordeaux* 1937 37 474
- BRADY, R. L. Lapine arborescent des guaines tendineuses. *Chir d organs de mouvement* 1924 9 25 244
- BURR, Case report 1 meeting of the board of the Chicago de Paris, 800 Ball et méso Sac de chir 186 342
- BRUNER, A. C. Benign xanthic extracapsular tumor of the extremities containing foreign body giant cells. *Ann Surg* 9 7 572-63
- BROWN, M. S. and MILES, A. E. Interpretation of tendon and tendon sheath. *Surg Gynec & Obst* 930 30 397-406
- BROOKS, E. J. D. Tumors of tendon and tendon sheaths. *Brit J Surg* 9 3 474-474
- COOPER, M. B. Squamous cell sarcoma of tendon sheath report of case. *J Bone & Joint Surg* 23 14 (2) 372-76
- DOR, LOUIS. Relations des tumeurs myélopiaques et des xanthomes. *Congr franç de chir* 504, 553-56
- DRAKE, T. L. Two tumors, cellular pleural delle guaine tendinee. *Chir d organs de mouvement* 1912 7 302-303
- FISKE, D. Giant-celled tumors of tendon sheaths. *Am J Surg* 809 7 20-123
- FLEISZIG, L. W. Giant-cell growth of bone and tendon sheaths. *Ann Surg* 9 8 66 426-49
- FLEISZIG, J. Über die bisher als Riesen-Zell-Tumoren (myeloiden) bezeichneten Granulationsgeschwülste der Sehnenhüllen. *Deutsche Zeitsch f Chir* 1924 24 239-265
- GONZALEZ AGUILAR, J. Contribution to the pathology of tendon tumors of giant cells. *J Bone & Joint Surg* 1935 (2) 10-18
- Idem. Interpretation patologica de los tumores de las tendones. *Crón méd mexicana* 20 417-44
- Idem. Interpretacion patologica de los tumores de las tendones de los tendones. *Rev méd de Mexico* 1930 30 524-529
- GRUBER, D. Über die Riesen-Zell-Tumoren der Sehnenhüllen. *Centralbl f allg Path* 30 1921 7 33 34 347
- GUTH, T. P. and STEWART, M. J. On myeloid tumors of tendon sheaths, 11th report of case. *Chirurgia 31* 9 8 133-139
- HARRIS, F. Tumors with xanthoma tissue. *Varh Mag f Lægerendok* 9 3 20 32 165
- Idem. Tumors of tendon sheaths giant capsules and multiple xanthoma. *Arch Path & Lab Med* 1927 4 507-51
- HART, M. A. Myeloid des guaines tendineuses. *Arch g de méd* 50 7 23 31 30-34
- HITCHIN, W. J. W. T. A. and CHODURA, H. R. Report on cases of xanthoma multiplex group.

- before the Pathological Society by Mr James Startin and Dr Stephen Mackenzie Tr Path Soc, Lond, 1882, 33 376-384
- 5 JANIK, A Tumors of tendon sheaths Ann Surg, 1927, 85 807-811
  - 9 JEBENS, E H Myeloma of tendon sheath Proc. Roy Soc Med, Sect. Orthopedics, 1932, 25 1093-1099
  - 30 KING, E S J Concerning the pathology of tumours of tendon sheaths Brit J Surg 1931, 18 504-517
  - 31 KNOWLES, I C, and FISHER H N Xanthoma tuberosum multiplex in childhood with visceral and tendon sheath involvement. J Am M Ass, 1921, 77 1557-1560
  - 32 KROGILS, A Zur Kenntnis ders g Xanthosarkomeder Sehnenscheiden Acta chir Scand, 1922, 55 363-383 Abstracted in J Am M Ass 1923, 80 592
  - 33 KURTZ, A D Xanthoma of tendon sheath Am. J Surg, 1919, 7 862-864
  - 34 KUSNETZOWSKY, N J Ein Fall multipler xanthomatöser Granulome der Sehnen Arch f klin Chir, 1923, 124 73-80
  - 35 LEVY G Xanthelasma et xanthome Ann d anat path, 1925, 2 247-282
  - 36 LEWIS, DEAN Tumors of the tendon sheaths Surg, Gynec & Obst, 1934 59 344-349
  - 37 MASON, M L and WOOLSTON, W H Isolated giant cell xanthomatic tumors of the fingers and hand Arch Surg, 1927 15 499-520
  - 38 McWHORTER, J E, and WEEKS, C Multiple xanthoma of the tendons Surg, Gynec. & Obst., 1925, 40 199-206
  - 39 MORTON, J J Tumors of the tendon sheaths Surg, Gynec. & Obst., 1934 59 441-452
  - 40 OLLERENSHAW, R Giant-celled tumours of tendon associated with xanthelasma Brit. J Surg 1923, 10 466-468
  - 41 PAOLUCCI, F Sui cosiddetti tumori a mieloplasi delle guaine tendinee Ann ital di chir 1929, 8 831-848
  - 42 PATEL Osteomes developpes dans les tendons d'Achille Lyon chir, 1931, 28 351-352
  - 43 PICK and PICKUS Weitere Mitteilung zur Lehre von den Xanthomen die echten xanthomatösen Neubildungen Arch f Dermat u Syph, 1910, 99 465
  - 44 PICKUS and PICK. Zur Struktur und Genese der symptomatischen Xanthome Deutsche med Wehnschr, 1908, 34 1426-1430
  - 45 PYBUS F C A note on a case of myeloma of the tendon sheath Brit. J Surg 1917, 5 172-173
  - 46 RAGINS, A B Benign tumors of the tendon sheaths of unusual size Ann Surg 1931, 93 683-690
  - 47 ROMITI Z Conoscenza dei sarcomi delle guaine tendinee Arch ital di chir 1925 12 406-428
  - 48 ROSENTHAL, I, and BRAUNISCH, R Xanthomatosis und Hypercholesterinämie Ztschr f klin Med 1921 62 429-441
  - 49 SCIGLIOSI, F Contributo allo studio dei tumori benigni delle guaine tendinee Chir d organi di movimento, 1931, 15 530-542
  - 50 SEROVI, J and LOMBART, A Les tumores de mioplaxias de las vainas tendinosas estudio histologico de dos casos Arch de med, cirug y especial, 1928, 28 10-17
  - 51 STYLIR Ueber xanthomatische Granulome Arch f path Anat, 1922, 239 20-31
  - 52 SILBERBERG, M Xanthome and Xanthoblastome. Arch f path Anat, 1925 254 56-62
  - 53 SPIESS P Zur Lehre der von Sehnenscheiden und aponeurosen ausgehenden Riesenzellensarkome ("Tumours myeloides" und "Myelome" der Autoren) Frankfurt Ztschr f Path 1913 13 1-44
  - 54 SPRENGER, W Zur Kenntnis der xanthomatösen Riesenzellgranulome der Sehnenscheiden Arch f klin Chir 1923, 169 683-687
  - 55 STEWART, M J Xanthoma and xanthosis Brit M J, 1924, 2 803-890
  - 56 STEWART, M J, and FLINT E R Observations on the myeloid tumour of tendon sheaths Brit. J Surg, 1915, 3 90-99
  - 57 STRAUSS, A Lipoma of the tendon sheaths with report of a case and review of the literature Surg Gynec. & Obst., 1922, 35 161-171
  - 58 TOROK L De la nature des xanthomes Ann. de dermat et de syph, 1893 s 3 4 1109-1156
  - 59 TOURNET, J P Le diagnostic des tumeur malignes des gaines tendineuses Progres med, 1920, 35 215
  - 60 Idem Les sarcomes des gaines tendineuses Rev de chir 1913, 47 817-854
  - 61 VILDONT P Lipoma arborescenta sistemico delle guaine tendinee della mano e del piede. Chir d organi di movimento 1931, 15 509-529
  - 62 VAN DER BEKEN, C A propos d'un cas de tumeur a myeloplaxies des gaines tendineuses. J de chir et ann Soc belge de chir, 1922, 31-29 27-31
  - 63 VISUDIVAN, A, and PAI M M Benign giant cell tumors of tendon sheaths Madras M J, 1931, 13 31-34.
  - 64 WEBER, F P Cutaneous xanthoma and "xanthomatosis" of other parts of the body—pituitary xanthomatosis—"xanthomyelomata" of tendon sheaths, etc.—and the 'cholesterin diathesis.' Brit. J Dermatol., 1924 36 335-370
  - 65 WHITE, J R Arborescent lipomata of tendon sheaths, a report of two cases Surg Gynec. & Obst., 1924, 38 489-490

## ACUTE INFLAMMATION OF THE PANCREAS

## A CAUSE OF EPIGASTRIC PAIN IN GALL-BLADDER DISEASE AND OF RECURRENT PAIN AFTER CHOLECYSTECTOMY

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THE rôle of the pancreas in the production of symptoms in patients with gall-bladder disease, has generally been considered an infrequent and insignificant one, or has been overlooked entirely. On the other hand, the fact that patients, after removal of a diseased gall bladder, sometimes have recurrence of symptoms has disturbed surgeons even when it has not been due to a stone left in the common duct. While it is not the purpose of this paper to present the problem of recurrent pain after cholecystectomy, it will record evidence which points to the fact that pancreatitis may be one of the reasons for its production. This data also suggests that the pancreas may be a frequent cause of symptoms even when obvious disease of the gall bladder is present. It is believed, moreover, that while such pancreatic inflammation may be a mild type of acute pancreatic necrosis, much evidence points to the fact that it is an entirely different lesion, an idea expressed several years ago by D. F. Jones. At any rate this form of acute inflammation of the pancreas was tentatively called acute interstitial pancreatitis and its relation to gall-bladder disease was suggested in a previous paper (4). Additional observations of this association will be recorded herein.

## PREVIOUS OBSERVATIONS

Of the considerable literature on the association of pancreatic and gall-bladder disease practically all of it concerns chronic inflammation. Reports of acute pancreatic disease are confined almost entirely to cases of frank necrosis, although of course this lesion though rare is frequently associated with gall-bladder disease. The importance of acute inflammation of the pancreas without actual necrosis (acute interstitial pancreatitis) was pointed out in the paper referred to (4) in which, of the 37 cases reviewed, it seemed probable that over half had an associated cholecystitis.

The many references in the literature to chronic pancreatitis are of value; the present study in so far as this designation represents a lesion which may be the result of repeated attacks of acute pancreatitis, an inference for which there is some evidence.

Mayo-Robson was probably the first to record the observation that he palpated an enlarged indurated pancreas during the course of gall bladder operation. His first case was operated on in 1890, and by 1904, 23 operations for this lesion were carried out (16). The indications for operation in the early cases (5) were obstructive jaundice, wasting, paroxysmal attacks of pain and some like sources having given rise to the suspicion of gall stones. Stones were, however, absent in half of the cases. The inferences seemed justified, therefore, at least in these, that it was the pancreatic lesion which was causing the symptoms. Drainage or division of the bile by cholecystostomy or cholecystenterostomy (plus removal of stones, here present) cured most of these patients. Follow up study showed that 87 are living and well, the 5 deceased either did not respond, still had symptoms of disease, or had died. The pancreatic lesion was confirmed at autopsy by microscopic examination in one or two cases and was called chronic interstitial pancreatitis. It is suggested, however, that some of these cases may have started as subacute or acute forms. In 93, the literature was fully summarized in the monograph of Hans Kehr. There neither placed the incidence of the hard indurated pancreas at 50 per cent of his cases. In both operations was done and in both stone was present in the common duct, but at only 5 per cent of cases in which stones were confined to the gall bladder. He claimed that there was nothing characteristic of the pain in patients who had pancreatitis as at first he to the gall bladder lesion. In contrast to Quirk, who believed, and cited 8 cases, that the localization of the pain in the mid epigastrium with radiation to the left shoulder blade, and the back in between the shoulder blades pointed to involvement of the pancreas. Galeis pointed out, moreover that in patients with pancreatitis the attacks were apt to be short, of 1 to 3 hours' duration, and were accompanied and followed by deep tenderness over the region of the pancreas.

Opes wrote that chronic interstitial pancreatitis is seldom associated with such definite symptoms that it is recognizable during life and even at autopsy the condition is frequently overlooked. Nicoll, in 1910, claimed that chronic pancreatitis may simulate cholecystitis, ulcer, or appendicitis. He performed and advised biopsy of the pancreas during operation in order to establish the diagnosis through microscopic examination. In one of his cases, operated on 5 days after onset of acute symptoms (the diagnosis was intestinal obstruction or perforated ulcer) the only lesion found was an indurated pancreas removed by multiple areas of fat necrosis. This case is similar to others already reported (4).

There are many other records of the incidence of pancreatic lesions noted during the course of gall-bladder operations.

Juhl, in 9, for example, found 147 instances of pancreatitis among 1,900 patients operated on for gall bladder disease (16.8 per cent). The diagnosis was based on the findings: 1 operation, 1 enlargement of the pancreas.

especially of the head, hardness sometimes of the whole gland, lobulation, and often edema. Of the 347 cases only 48 were described in detail, 46 had stones, 8 in the common duct, in 15 the common duct was drained. Follow up after 1 year showed 30 well (3 had attacks of diarrhea), 2 unimproved, and 16 were not heard from. Analysis of the clinical histories in the entire group of 347 cases did not reveal any special symptoms pointing to disease of the pancreas

Of perhaps more significance is the incidence of pancreatitis in gall-bladder cases not relieved by cholecystectomy

The most complete study of recurrent pain after cholecystectomy was written by Talman. Although pancreatitis was discussed as one of the prominent causes, he recorded the general belief that there was nothing characteristic in the clinical picture of those cases of gall-bladder disease which at operation also disclosed pancreatitis. However, he also called attention to the inaccuracy of a diagnosis of pancreatic involvement based merely on palpation at operation. This was apparent from the variable incidence of the lesion as reported by many surgeons, figures between 9 and 81 per cent were found of the frequency of pancreatic disease in gall bladder cases. The error, of course, may be in both directions, i. e. definite pancreatitis may be missed and the gland reported normal or an enlarged head described due to a thick fatty mesentery through which a normal gland is felt. Nicoll believed that actual biopsy of the gland is necessary to make a diagnosis. Certainly in specimen or palpation of the visible gland should increase considerably its accuracy.

Douglas recently reported a number of cases, 3 of which "after cholecystectomy for cholelithiasis had epigastric or left hypochondric pain of varying degrees, which was believed by the operator to have been mild attacks of pancreatitis." In another patient operation revealed a hard indurated pancreas, fat necrosis, and stones in the gall bladder. Recurrent pain occurred 3 weeks after operation but the pain disappeared after the re establishment of bile drainage.

### PRESENT OBSERVATIONS

In all, 6 cases will be described, in 5 of them the evidence of pancreatitis is anatomically conclusive, in the other one merely presumptive. The

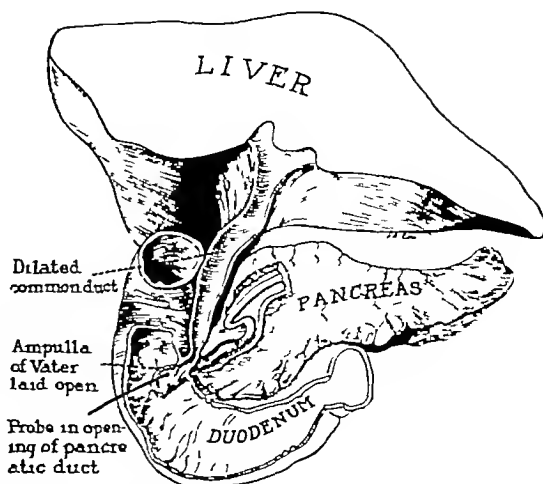


Fig 1 A drawing of autopsy specimen in Case 1. Note the narrowing of the dilated common duct at its lower end as it passes through the head of the pancreas. The termination of the pancreatic duct is well within the common duct inside the sphincter of Oddi (ampulla of Vater). The same arrangement was found in the other autopsied case (Case 6).

clinical histories are given. Table I summarizes the most important findings.

**CASE 1.** L. M., 58 year old housewife entered Barnes Hospital (No. 23763) first on January 1, 1930, complaining of severe attacks of epigastric pain going through to her back and around the costal margin to the right shoulder, lasting several hours, and not relieved by medication. A barium meal and gastro-intestinal X-ray series were negative, but a cholecystogram showed no shadow. On admission she was still suffering from an attack of the previous day and on examination showed tenderness and muscle spasm and guard in both upper quadrants, especially on the right. The other examinations were negative, temperature and pulse were normal. At operation the

TABLE I—SUMMARY OF CASES OF PANCREATIC INFLAMMATION

Case	Age Sex	Location of pain	Tenderness	Jaundice	Pancreatic lesion	Gall bladder	Stones	Blood amylase	Outcome
1	58 F	Epigastrium right and left hypochondrium	Over pancreas (X-ray)	+	Fat necrosis A.I.P.*	Cholesterosis	o	?	Recurrent pain after cholecystectomy secondary operation death
2	57 F	Epigastrium left sided once	Epigastrium and to left	o	Fat necrosis A.I.P.	Chronic inflammation	+	?	Cholecystectomy cysticocholedochostomy cured
3	38 F	Epigastrium left and right radiation	Left hypochondrium	+	?	Chronic inflammation	+	+	Recurrent pain after cholecystectomy
4	30 F	Epigastrium distention	Epigastrium	+	Fat necrosis	Chronic inflammation	+	+	Cholecystectomy cysticocholedochostomy cured
5	34 F	Left hypochondrium distention	Epigastrium and left hypochondrium	?	Hard induration and edema	?	?	?	Recurrent pain after cholecystectomy Secondary operation Subsidence of attacks
6	54 M	Around umbilicus	Diffuse	+	A.I.P. abscess	Chronic inflammation	o	?	Death after cholecystectomy

\*A.I.P.—acute interstitial pancreatitis as shown by microscopic section

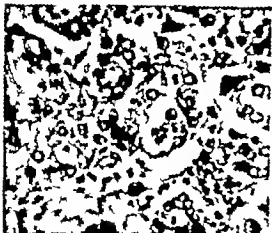


Fig. 1. Photomicrograph of the pancreas in Case 1. The upper view is the low power and represents extensive infiltration with polymorphonuclear leucocytes, some edema but no hemorrhage. The acinar cells are intact. Evidence of old fibrosis is also seen, indicative of previous attacks of inflammation. The lower view represents a higher magnification. Note the presence of leucocytes within duct as well as between acini.

next day the appendix and gall bladder were removed. A note was made as to the pancreas by the operator. Recovery was uneventful. The gall bladder on examination showed cholesterolemia (strawberry gall bladder) contained no stones, and on section showed some evidence of chronic inflammation. The patient's second admission was on November 6, 1933, about 514 years later. At this time she stated that the painful attacks were not relieved by her operation but began to recur 3 months after she left the hospital. They were not very severe until 4 months ago when she was awakened at 500 m. with pain which radiated bet. cen. the shoulder blades, and she panicked clear fluid. This attack subsided but no other attacks occurred, the last one the day before admission. Jaundice was observed and there was loss of 25 pounds in weight. Examination disclosed moderate arteria (normal base



Fig. 2. Photomicrograph of biopsy specimen of pancreas in Case 2. The upper view is lower power magnification and shows extensive infiltration with polymorphonuclear leucocytes, some edema, but no hemorrhage or necrosis. Slight fibrosis was present indirectly of previous inflammation. The lower view shows, under higher magnification, several polymorphonuclear leucocytes within the lumen of duct with debris surrounding edema.

stained, xiric index 3, was den. Bergh reaction—no medulla direct and parietal indirect. Last bowel cells 8,500 pulse and temperature normal. There was post-operative hernia through which marked tenderness was elicited. On deep pressure through this defect, the pain was increasing. Under the fluoroscope after barium meal, the duodenal curve was evidenced indirectly of pancreatic disease suggestive of carcinoma, although the extreme tenderness which was localized over this area prevented palpation of mass.

At operation, risk after admission, the common duct was opened, but no stone was found. The pancreas was enlarged and firm. During the exploration the patient's circulation began to fail and in spite of all resuscitative

exodus occurred. At autopsy the pancreas was sectioned and found to be the site of extensive acute inflammation besides much old fibrosis. Numerous areas of fat necrosis were seen in the capsule. The cells of the pancreas itself, however, were intact (Fig. 2). No carcinoma was present. The common duct was slit open and found to be dilated but contained no stones and was narrowed for several centimeters as it passed through the head of the swollen pancreas. In its lumen about 3 or 4 millimeters above the sphincter was the opening of the main pancreatic duct (Fig. 1). Section of the common duct and duodenum showed no acute lesion. The liver was normal grossly and microscopically except for occasional nests of round cells in the perportal areas.

CASE 2. M. G., 57 year old housewife, entered St. Louis City Hospital (No. 12512) October 27, 1933, with the complaint of intermittent attacks of epigastric pain with freedom during the intervals. The present attack began 10 days previously. On admission to the hospital, pulse, temperature, and leucocyte count were normal, there was extreme tenderness in the right and left epigastrium, most marked on the left. She vomited repeatedly and gastric analysis after a test meal revealed no acidity. Cholecystogram showed no shadow, gastro intestinal series after barium meal was negative. The attack subsided but on the fourth day recurred and a note was made by the senior interne that the "pain was on the left side just above the umbilicus and extending around to the left." Two weeks after admission and 2 days before operation I saw her in another attack and on cursory examination found tenderness in the mid-epigastrium and over the gall bladder area. Operation on November 11, 1933, revealed a gall bladder with many small stones, and an enlarged indurated pancreas. After cholecystectomy, the cystic duct was found patent and I explored the common duct of normal size, through it. A small stone similar to those in the gall bladder was fished out of the lower common duct. A bulb tipped probe was passed to the duodenum readily but it encountered a definite resistance at the ampulla. I sewed a catheter into the cystic duct. The pancreas was then exposed through the gastrocolic omentum and the organ inspected over most of its length. Numerous white areas of fat necrosis were distributed over the capsule of the gland and the immediate fat surrounding it. The parenchyma was of a much paler pink color than normal, and the entire gland was indurated and hard especially at the head. I removed a portion of the pancreas for biopsy (Fig. 3) from the body of the gland and closed the defect with sutures, there was slight bleeding and only momentary escape of pancreatic juice.

Drainage of bile continued for 11 days when the tube came out, and then drainage ceased. Recovery was uneventful. Patient has been free of symptoms since then (1 year).

CASE 3. L. B., housewife, age 38, entered St. Louis City Hospital (No. 13657) for the first time on October 6, 1933, with onset 3 days before consisting of pain in the left side radiating to the right side and then over the entire abdomen, she vomited repeatedly. Opiates relieved the pain hardly at all. On admission to the hospital she was tender only over the right upper quadrant, pulse, temperature, and leucocyte count were normal. Cholecystogram showed no shadow. A diagnosis of cholecystitis was made. At operation (October 24, 1933), the gall bladder was found to contain a few stones. Cholecystectomy was followed by an uneventful recovery. No note was made by the operator as to condition of the pancreas or common duct.

She was admitted again on November 16, 1933, a week after discharge, with recurrence of the same pain that she had had before operation. She pointed to the left of the

midline and had pain also in the small of the back. The attack was about over when she was admitted to the hospital and she was discharged 3 days later. The sclerae were questionably icteric.

Her third admission was 1 week later, 12 hours after the onset of another severe attack. The pain and tenderness were localized to the left hypochondrium and radiated to the back, but later was felt also on the right side and right shoulder. I saw her the next day and she was in obvious distress and was vomiting repeatedly. The white count was normal. The pancreatic area could be easily felt through a wide diastasis of the rectus muscles and was definitely tender both to the left and right of the midline. Although her sclerae were not icteric, blood serum examined at this time was distinctly yellow, though its bilirubin content unfortunately was not measured. The blood amylase at this time (24 hours after onset of the attack) was 75 units (normal is 5, according to technique previously described) (5). Two days later a second specimen contained but 20 units. Although the plasma was less yellow in color its icteric index was 13, the van den Bergh showed a delayed direct and positive indirect reaction. By December 4 (6 days after admission), the blood amylase was normal (5 units), and the serum of normal color.

During this time the symptoms gradually and completely disappeared. The temperature dropped from 38.5 degrees C (101.4 degrees F) to normal and the pulse from a rate as high as 148 to normal. On discharge she was urged to eat frequently to maintain a steady flow of bile and aid in keeping the biliary tract open. She has had no recurrence of pain (6 months).

CASE 4. A. S., a housewife, age 39 years, was admitted to St. Louis City Hospital (No. 8597) with a history of recurrent epigastric pain for the past 3 years accompanied by vomiting and jaundice. The present attack, the most severe of all, began 2 days ago. The pain did not radiate. Examination revealed an obese woman in severe pain, vomiting repeatedly, with a tense distended abdomen, tender however only in the mid-epigastrium. The sclerae were slightly yellow. Temperature was 37 degrees C (98.4 degrees F), pulse, 70, respiration, 20, white blood count, 18,000. Blood amylase was ten times the normal value. Icteric index was 12, van den Bergh, slightly positive, direct, delayed. Under conservative care, pain and vomiting gradually subsided and with it the blood amylase returned almost to normal 4 days later. Cholecystogram revealed no shadow. At operation a chronically inflamed gall bladder containing several stones was removed and the common duct explored through the open cystic duct which was then drained by sewing a catheter into it. The pancreas felt hard and enlarged. When it was exposed through the gastrocolic omentum numerous pinpoint areas of fat necrosis were seen, biopsy was done, section showed the acuteness of the lesion, whereas the gall bladder revealed only chronic inflammation. The postoperative course was uneventful, the cystococholodochostomy tube drained bile for a week, came out, and the wound closed spontaneously. Patient has remained free from symptoms.

CASE 5. Female, 1/2 age 34 years, entered the hospital on January 20, 1932, complaining of sudden and extremely severe pain in the upper left abdomen which came on the day before, after eating a hearty evening meal. The pain radiated around to the back and the left of the chest. Morphine gave no relief. Vomiting was frequent. She had had previously two similar, severe attacks, and many less severe and of shorter duration. The patient had been operated on about 8 years ago for appendicitis and cholecy-

<sup>1</sup>Details of this case were kindly furnished by Dr. Raymond L. Zech, Seattle, Washington.

still, at which time the gall bladder was drained. Six years later (7 years ago) it was removed. No information was available as to the condition of the pancreas.

Examination revealed marked tenderness in the epigastrium and left hypochondrium. Rigidity was confined to the left upper abdomen and epigastrium. The temperature was 37 degrees C. (90 degrees F.) pulse, plus 80. In spite of the extreme pain and tenderness, she did not appear distressed. On January 30, 1935 a blood count showed hemoglobin of 74, erythrocytes 3,900,000 and leucocytes 9,000 polymorphonuclears, 65 and mononuclears 35. Calcium chloride was given intra-venously (5 grains) with no relief of pain. Morphine (1/4 grain) gave only slight relief. The next day the leucocyte count was increased to 12,500 polymorphonuclears 82 and mononuclears 18. Pain was still severe and the patient started to vomit, but this did not continue long. The following day the leucocyte count was but 7,050 with polymorphonuclears 56 and mononuclears 44. Blood chemistry analysis showed blood chloride, 245.5 grams blood sugar, 7 milligrams. Diastatic index (Sayer and Kilham technique) was 26 milligrams (normal). Plain X-ray plate of the abdomen was negative. From the history of repeated attacks, the characteristic pain associated with vomiting which was not local in nature, the tenderness confined to the region of the pancreas, the characteristic and localized rigidity and the history of the previous operations, diagnosis of acute pancreatic necrosis was made, and an operation was advised. The patient, however, refused further surgery. On January 3, she started to improve and was discharged on January 27, 1935 (1 week after admission) following which she had one or two short attacks of pain in spite of diet almost entirely free from fat. On her next admission, August 8, 1935, during another attack, considerable abdominal distention was present. The tenderness and rigidity were most marked over the left upper quadrant. At operation no intestinal obstruction was noted, the bile ducts were negative. The duodenum was adherent to the liver. Through an opening in the gastrocolic omentum the pancreas was exposed and found to be enlarged and thickened throughout and edematous to appearance. Recovery was uneventful and the patient after discharge reported that attacks recur every 3 or 4 months but are not so severe, though they do confine her to bed for a few days each time.

CASE 6. W. R. salesman, age 54 years, was admitted to St. Louis City Hospital (N 10074) January 10, 1934 six months before he had an attack of indigestion which subsided, to recur in December this time with pain around the umbilicus and posterior which became severe and was accompanied by clay colored stools, it subsided in 2 weeks. The patient did not stop his work. Jaundice recurred days before admission, and he had chills, fever and pain around his umbilicus which did not subside. Examination revealed the patient ill and markedly jaundiced (icteric index 42) with the abdomen slightly distended, but tender and resistant everywhere especially in the right upper quadrant. Pulse rate was 70 temperature, 37 degrees C. (98 degrees F.), although it did reach 38.5 degrees C. (101 degrees F.) on one occasion. The leucocyte count was 7,200, bleeding time 3/4 minute and clotting time 13/4 minute. My impression was acute cholecystitis with stone in the common duct. The acute process subsided rapidly and his jaundice, pain, and rigidity cleared up completely within 1 week. At operation January 23, I found shrunken gall bladder containing no stones. The common duct was dilated, after cholecystectomy I explored it through the patient's cystic duct, but no stones were found. A metal probe entered the duodenum but only after passing definite resistance at the ampulla. The liver was small and

chrudic, the spleen was soft and three times its normal size. The pancreas felt enlarged and indurated. An attempt to expose the gland through the gastrocolic omentum was given up because of the extensive adhesions joining the two structures and because marked bleeding was encountered. I sewed a catheter into the cystic duct for drainage. The bile was clear and amber in color and drained profusely during and after operation. A transfusion of 500 cubic centimeters of blood had been prepared ahead of time and was given at the conclusion of the operation although his general condition was good. It remained so for 36 hours when he suddenly became cyanotic, weak, heart sounds distant, developed rales in his chest, and expired 6 hours afterward. At autopsy there was found pulmonary edema and extensive arterial disease of the aorta. A few people passed in the common duct by the pathologist was found to enter the pancreas directly also, as was found after dissection, in the fact that the pancreatic duct opened into the common duct several millimeters above the sphincter, which was tight and contracted. No stones were found anywhere. The pancreas was large, firm, and adherent everywhere. The cut section showed small abscess in the head near the dorsal surface and surrounded by several smaller abscesses. No hemorrhage, gangrene, or infarction in the pancreas itself were found. There was no fat necrosis. Sections of the gland show of an acute picture similar to that of Case 5 and. There was no ductolith and the common duct showed only an old fibrotic dilatation, with no leucocytic cells. The liver showed chronic biliary changes. The tissues unfortunately was allowed to develop postmortem changes which made the microscopic sections unsuitable for obtaining adequate photomicrographs.

### DISCUSSION

Six cases of acute inflammation of the pancreas are described, the diagnosis being based in 5 by anatomical proof (3 at autopsy 2 by biopsy, and by direct inspection at operation) and in the other by the recurrence of rather characteristic pain after previous cholecystectomy (during which there was an increased blood amylase). All were patients with proved gall-bladder disease. 3 had had a cholecystectomy but returned with recurrent pain, the 3 others were operated on for gall-bladder disease, 2 with and the other without stones. Clinically the location of the pain and tenderness in the mid and left epigastrium over the pancreatic area in 4 cases suggested rather definitely inflammation of this gland. The blood in 2 patients was found to contain a high amylase content.

The importance of pancreatic involvement in gall-bladder disease has generally been denied, for it has been assumed that the lesion is silent and that it has only theoretical interest. The fact, however, that such a lesion may be responsible for recurrent pain after cholecystectomy gives it definite practical importance. The observations recorded herein point to such an association and when taken with data previously recorded (4) emphasize the dominant part that the pancreas

may play in the production of epigastric pain, not only when disease of the gall bladder is also present or has been removed but also in cases in which it contains the only abdominal lesion. The evidence also indicates that pancreatitis is far from silent and that the symptoms it causes are frequently characteristic and often easily distinguished from those produced by gall-bladder disease alone. The fact, finally, that knowledge of the pathogenesis of this type of pancreatic inflammation is still incomplete should stimulate further study in order that adequate measures for the prevention and treatment of the lesion might be instituted.

The term "acute interstitial pancreatitis" will be used in describing the lesion in the present cases since the microscopic sections in 3 of them (Cases 1, 2, and 6, Figs 2 and 3) showed the same inflammatory signs noted in those previously reported (4). These signs, briefly, consist of marked infiltration of acute polymorphonuclear cells into the interlobular as well as interacinar tissue. In addition such cells are frequently found within the lumen of the finer ducts suggesting a duct borne infection. At any rate the presence of these cells indicates an acute process, which is borne out by the occurrence of edema in many places. The presence of fat necrosis in 3 cases also points to the acute nature of the lesion. Nevertheless, one sees no evidence of the cell necrosis or hemorrhage characteristic of acute hemorrhagic pancreatitis even though in some cases the duration of the disease was long enough to have produced it. In addition to acute signs there was evidence of previous subsided inflammation in the frequent interlobular and interacinar fibrosis. In only 1 of these cases was there suppuration (Case 6) present.

The reasons for using the designation "acute interstitial pancreatitis," as distinguished from "acute pancreatic necrosis," were discussed in my previous paper (4). It is obviously impossible to say that we are dealing with two different diseases until the pathogenesis is better known. It may be that they represent the same disease in a severe and mild form. The striking difference in the clinical picture of acute pancreatic necrosis and the cases here presented seems sufficient to warrant separate consideration. Moreover, the apparent frequency of the present type of pancreatitis and its tendency to be overlooked in biliary disease would seem to justify, for the time being at least, considering it as a separate clinical entity.

Further comment on the present observations will be made as follows

## PATHOGENESIS

Of the many theories of the genesis of pancreatic inflammation that of regurgitation of bile into the pancreatic duct from the common duct has aroused the most interest. Such an event is made possible by the presence of an impacted stone in the ampulla. Unfortunately for this theory, a stone is not always present in these cases. Moreover, it has been shown by Mann and Giordano that the anatomical arrangement necessary for such an event is too infrequent to be of practical importance. The suggestion of Archibald that this reflux could occur even in absence of stone, by a spasm of the Oddi's sphincter, made the idea more plausible for the anatomical arrangement of the ducts is such in 20 per cent of humans that the common sphincter by spasm could conceivably convert the biliary and pancreatic ducts into a continuous channel. This could be achieved by even a tiny impacted stone in but 4 per cent of cases (Mann and Giordano).

This idea is supported by the autopsy findings on Case 1, for the pancreatic duct emptied into the common duct several millimeters proximal to the sphincter of Oddi so that bile could easily flow into the pancreas if the papilla were closed for any length of time. The microscopic section of the pancreas too showed acute inflammatory cells within the ducts (Fig 2). The same anatomical arrangement was noted at autopsy in Case 6, indeed, the pathologist who probed the common duct noted that it went directly into the pancreatic duct and not into the duodenum at all. It is of interest too that in Case 2, evidence of sphincter spasm was noted at operation by the temporary impediment offered a bulbous probe which was passed through it into the duodenum, and that the lumen of the pancreatic duct in the biopsy specimen also contained inflammatory cells (Fig 3).

Additional observations of a direct communication between the pancreatic and common ducts in cases of pancreatic disease is furnished by Nordmann who states that in 2 cases in which the gall bladder was drained pancreatic juice was demonstrated in the fluid draining from the cholecystostomy wound. Other examples have been mentioned before (4). The observations of Popper add further evidence of its importance. He found of 18 cases of pancreatitis. In a case described by R. M. Jones clear pancreatic juice flowed from a drainage tract placed at a local area of pancreatic necrosis. A communication with the biliary tract was shown by the presence of bile in the discharge after removal of the gall-bladder drain (10).



To drain bile for a short period of time or at least provide a by-pass for its escape is a rational procedure if we assume that bile may otherwise be able to enter the pancreas and continue the inflammatory process. Whether a short period of drainage has any permanent effect cannot at present be definitely stated. Diversion of bile by choledochostomy has the disadvantage that it adds to the mortality of the operation and in a few cases may lead to subsequent stricture. In Cases 2, 4, and 6, I established biliary drainage without opening the common duct by inserting a catheter into the cystic duct. This procedure, cysticocholedochostomy was used by Halsted in 1899 and others, according to Reid, who described the procedure in 1911. It was used by Reid to provide drainage after an incision in the common duct had been sutured. It was also described in 1915, by Lobinger. In itself it is a simple enough procedure unless, of course, the cystic duct is definitely occluded. Often, however the duct is large enough to permit exploration of the common duct and sometimes the hepatic ducts, differences being dependent, of course, on the manner in which it joins the biliary tract. In most cases, however if patent, it allows probing of the distal part of the common duct, the papilla, and the duodenum quite easily. Bile drainage through a cysticocholedochostomy ordinarily does not last long, often only a week or two, after which the tube comes out and the skin heals unless, of course, an obstruction is present. Prolonged bile drainage (for months) has been advocated by some surgeons, but can be achieved only by the insertion of a T tube in the common duct.

Another suggestion, that of actual dilatation of the sphincter of Oddi, merits some consideration and can, of course, be done by means of common duct probes armed with bulbs of increasing caliber. Further observations may show that this procedure is worthy of more extensive use. It can be readily done through the cystic duct, thus avoiding the necessity of opening the common duct, at least in most cases.

One may advise frequent feeding with the idea that otherwise intermittent stasis of bile is functional and may be disadvantageous in these cases. The fact that in several cases attacks came on after a heavy meal also should caution the patient in favor of small frequent feedings. By eating often, a more uninterrupted stimulus to both biliary and pancreatic secretion is effected, which may aid in keeping the channels open and perhaps eventually lead to a dilated sphincter.

There is apparently no necessity for an emergency operation in this type of pancreatitis since

the possibility of its developing into acute hemorrhagic pancreatitis, from the evidence thus far available, appears remote. We are dealing, it would seem, with either an entirely different disease and one morose or which can often be readily differentiated from pancreatic necrosis, or a mild type which does not go on to hemorrhage and necrosis. The indications for secondary operation in cases with recurrence after cholecystectomy are more difficult to evaluate. If further study shows a sufficiently frequent tendency to spontaneous subsidence of attacks obviously symptomatic treatment is all that is needed. If disability is great and intervention is decided upon, the procedure to be carried out is a difficult problem. Further knowledge of pathogenesis, whether it confirms the assumptions made herein or not, is of course needed. Continued bile drainage with a T tube has been recommended by some but it has obvious disadvantages. Dilatation of the sphincter might be tried through an opening in the common duct. It is suggested, finally that, in some cases, especially those with attacks of jaundice the portion of the pancreas surrounding the lower common duct be resected so as to prevent the biliary occlusion caused by swelling of the pancreas. Another possibility too is actually short-circuiting the bile away from the pancreas by implanting the common duct into the stomach or duodenum at a new site.

#### SUMMARY

Six cases with acute interstitial pancreatitis are presented as examples of the pancreatic origin of pain and jaundice in patients with gall-bladder disease (3 cases) and in patients with recurrent symptoms after cholecystectomy (3 cases). Evidence is presented that this lesion is an entity which produces a clinical picture which is characterizable and which is distinguishable from frank pancreatic necrosis. The value of blood amylase determinations in its diagnosis is shown. That it has a definite pathogenesis, which depends on an anatomical arrangement by which, during spasm of the sphincter of Oddi, bile may enter the pancreatic duct is indicated by additional evidence. The therapeutic indications which this lesion invites, aside from treatment of the associated biliary disease, are discussed.

#### BIBLIOGRAPHY

1. ARCHERDALL, E. *Ann. Surg.*, 1926, 90, 283.
2. BURROUGHS, O. *Best. J. Clin. Med.*, 1926, 39, 31.
3. DOUGLASS, J. *Ann. Surg.*, 1911, 93, 960.
4. ELMAN, R. *Surg. Gynec. & Obst.*, 1915, 57, 491.
5. ELMAN, R., ANDERSON, N. and GRABBE, E. A. *Arch. Surg.*, 1921, 9, 243.

- 6 GRAHAM, E A *Surgical Diagnosis* Vol 3, p 411, Philadelphia W B Saunders & Co, 1930
- 7 GRAHAM, E A COLE, W H, COPPER, G H, and MOORE, S *Diseases of the Gallbladder and Bile Ducts*. Philadelphia Lea and Febiger, 1928
- 8 GULEKE, N *Verhandl d deutsch Gesellsch f Chir*, 1912, 41 310 (Part II)
- 9 JONES, D I *New England J Med*, 1908, 109 710
- 10 JONES, R M *Brit J Surg* 1934, 22 296
- 11 JUDD, E S *J Am M Ass*, 1921, 77 197
- 12 KEHR, H *Chirurgie der Gallenwege*, p 759 Stuttgart, 1913  
idem. *Praxis der Gallenwege Chirurgie* Vol 2, p 374 Munich 1913
- 13 LOBINGIER, A S *J Am M Ass*, 1925, 85 85
- 14 MANN, F C, and GIORDANO, A S *Arch. Surg*, 1923, 6 1
- 15 MAYO-ROBSON, A W *Lancet*, 1900, 2 235
- 16 MAYO-ROBSON, A W, and CAMMIDGE, P J *The Pancreas, Its Surgery and Pathology* Chap 16, p 468 Philadelphia W B Saunders Co, 1907
- 17 NICOLL, J H *Brit M J*, 1919 2 625
- 18 NORDMANN *Verhandl d ges f Chir*, 1913, Part II, p 362
- 19 OPTER, E L *Diseases of the Pancreas*, 2d ed, p 208 Philadelphia, 1914
- 20 PORRER, H L *Arch. f klin Chir*, 1933, 175 660
- 21 REID, M R *Ann Surg*, 1921, 73 458
- 22 RUCE, E *Arch f klin Chir*, 1908, 87 47
- 23 TALMAN, I M *Arch f klin Chir*, 1933, 175 472

# THE TREATMENT OF SENILE VAGINITIS WITH OVARIAN FOLLICULAR HORMONE

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THE term *senile or adhesive vaginitis* describes a non-specific inflammatory condition often occurring during post-menopausal life. Its occurrence is not uncommon in young women in whom an artificial menopause has been produced by surgical or radiation castration. Since this condition is not limited to elderly women, but may also follow the cessation of ovarian function in young women, post-menopausal vaginitis would be a more suitable term.

## PHYSIOLOGICAL ATROPHIC CHANGES

The physiological atrophic changes which occur in the genital organs after an artificial or spontaneous menopause may be considered the normal sequel of the menopause. The general progressive atrophy of the genitalia during this period affects the vagina in that there is a shortening of the vaginal lumen and a constriction of its diameter particularly at the introitus. The vaginal vaults may disappear completely and the vaginal walls lose their elasticity and distensibility. These gross changes are due to a loss of elastic tissue and muscle cells in the musculature which are replaced by rigid connective tissue. The mucosa has a smooth and glistening appearance as the result of a loss of the normal rugae and the atrophic changes in the squamous epithelium. Excessive stretching of the mucosa on vaginal examination or the trauma of intercourse may lead to superficial mucosal abrasions and petechial hemorrhages.

These physiological changes may develop very slowly over a period of years, becoming more marked with advancing age. Occasionally an abrupt onset of the menopause in a young woman by removal of the ovaries or radiation castration may produce a rapid development of atrophic changes. The physiological changes may cause the production of no local symptoms other than a dyspareunia.

The squamous epithelium on histological examination consists of only five or six layers of cells. The functionalis has disappeared entirely and there is no evidence of cyclical activity. The cells of the basalis are small and the nuclei and granular cytoplasm are dark on staining. The basal layer of cells is less distinct than during active sex

life. Little evidence of cellular activity can be seen.

## SENILE VAGINITIS

The development of *senile vaginitis* follows an inflammation superimposed on the physiological atrophic mucosa of the vagina. The exciting factor may be an irritating uterine discharge which macerates the atrophic vaginal epithelium, or a recurring minor trauma which injures the low inactive squamous epithelium. The usual pathogenic organisms in the vagina invade these denuded unprotected areas and start an inflammatory process. The organisms involved are variable and probably of low virulence. The inflammation may cause superficial ulcerations or erosions of the vaginal mucosa. Grossly they appear as small, punctate, superficial hemorrhagic areas. The denuded areas become fixed together when in apposition if the process is extensive, forming firm adhesions which finally organize to form firm adhesions or synechiae. The cervix may be hidden by these adhesions if they are numerous and rarely the continuity of the vaginal lumen may be lost. This adhesive process is the healing stage of the disease. Thus, *adhesive vaginitis* is a late stage of *senile vaginitis*. The condition may become entirely quiescent, but complete obliteration of the vaginal vaults and a large portion of the lumen may be an end-result.

## SYMPTOMS

The symptoms of vaginitis are vaginal discharge and burning, pelvic pain and discomfort, smarting on urination, and occasional pruritis of the vulva. The discharge is usually watery in consistency grayish-white, and occasionally seromucous, which may be suspicious of cancer. The discharge is usually scanty in amount but may be profuse at times. Its irritating character may cause an inflammation of the vulva and urethra, extending over the perineum and onto the groin. Exacerbations of the condition may aggravate the symptoms to such an extent as to cause loss of sleep.

## DIAGNOSIS

Senile vaginitis is not difficult to diagnose. A subacute or chronic vaginitis developing during

# DAVIS THE TREATMENT OF SENILE VAGINITIS

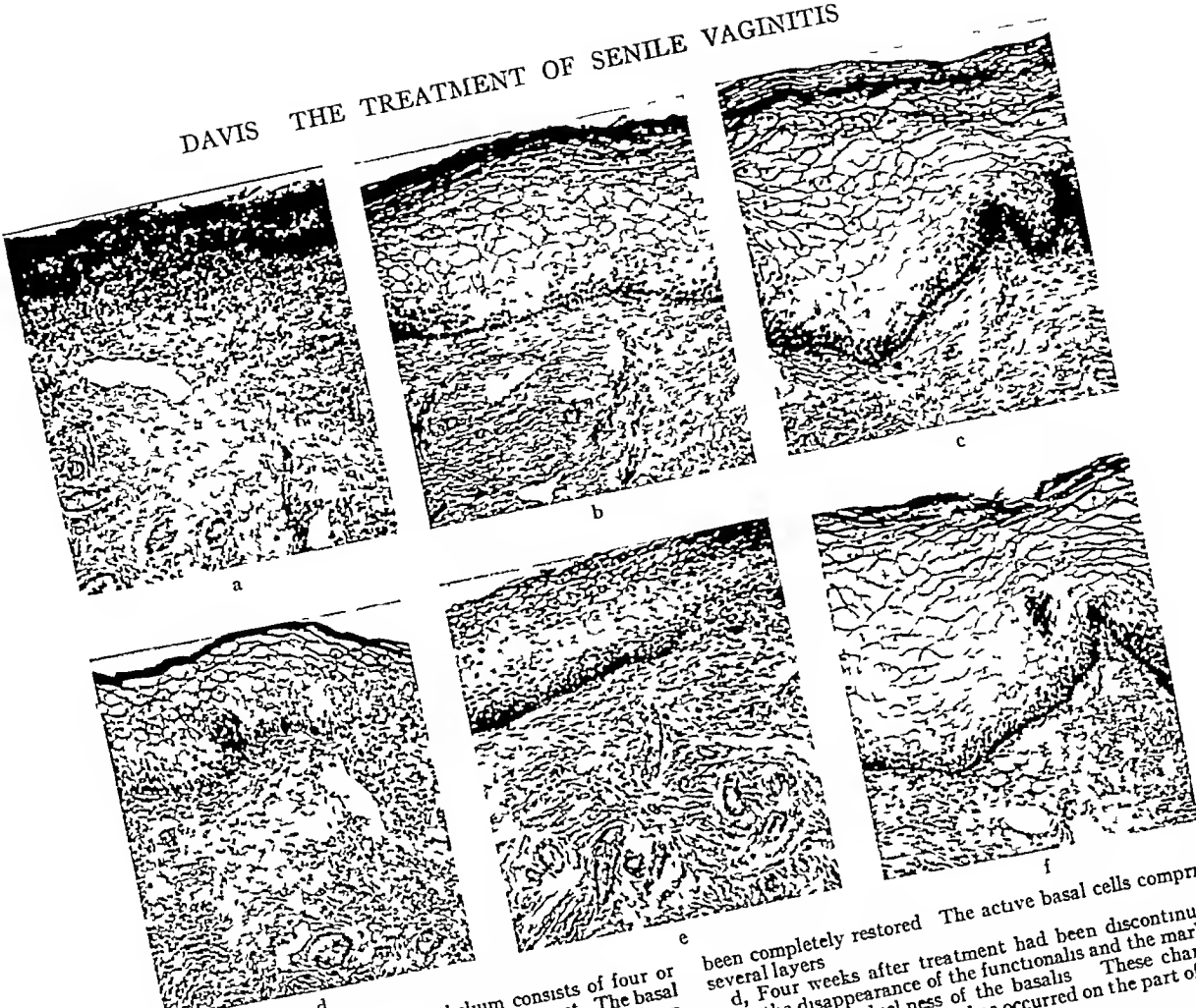


Fig. 1 a, The squamous epithelium consists of four or five layers of cells which are small and indistinct. The basal layer of cells is somewhat irregular. There is no sharp demarcation between the cells and the subepithelial zone. No mitotic figures can be seen. A moderate infiltration of round cells and a few polymorphonuclear leucocytes can be seen in the subepithelial zone, indicative of the inflammatory condition.

b, Note the complete restoration of the squamous epithelium to that seen during active sex life. The basal cells are arranged regularly and show signs of cellular activity. All of the cells are large, clear, sharply demarcated, and contain an abundance of glycogen. The functionalis is beginning to develop. Note the increased vascularity of the subepithelial connective tissue and the complete disappearance of inflammatory cells.

c, Six weeks after treatment. Note the increasing thickness of the squamous epithelium. The functionalis has been completely restored. The active basal cells comprise several layers.

d, Four weeks after treatment had been discontinued. Note the disappearance of the functionalis and the marked decrease in the thickness of the basal layer. These changes demonstrate that regression has occurred on the part of the epithelium.

e, Nine weeks after treatment had been discontinued. Note the continued regression of the squamous epithelium, the complete disappearance of the functionalis and partial destruction of the basal layer. The cells have again decreased in size and all signs of cellular activity in the basal zone have disappeared.

f, The squamous epithelium has been rebuilt to this stage after reinstitution of amniotin treatment for a period of 3 weeks. (All photomicrographs were magnified 425 times for accurate comparison of the squamous epithelium.)

the postmenopausal period is usually of this type. Digital examination frequently reveals the vaginal walls adherent in places by filmy adhesions which may be broken up easily. The vaginal lumen is greatly narrowed and inelastic. Simple examination causes pain and bleeding. Speculum examination reveals a smooth, glistening mucosa

with small foci of superficial hemorrhage and loss of epithelium. The introitus may be reddened and irritated, and the inflammation may extend over the perineum and about the anus. The glue-like discharge on microscopic examination consists of epithelial cells, leucocytes, red blood cells, and a host of bacteria. Occasionally, the tri-

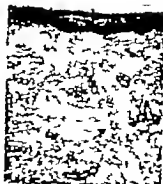


Fig. 5. Note the low atrophic squamous epithelium. The cells are small, densely packed together and their ori-

lines are indistinct. The basal cells merge indistinctly with the underlying connective tissue.

b. Three weeks after treatment. Note the complete restoration of the squamous epithelium to that seen during active sex life.

c. Four weeks after treatment had been discontinued. The squamous epithelium has regressed to the atrophic type seen in Figure 5a.

d. Three weeks after discontinuation of treatment. The squamous epithelium again has been rebuilt. Note the numerous blood vessels in the sub-epithelial zone.

e. The process has greatly increased in thickness. The basement layer is stopped on well defined bands. Note the activity manifested in the basal layer of cells.

(All photomicrographs are magnified 415 times for accurate comparison of the squamous epithelium.)

chronous parasite is found complicating the varied bacterial flora. It is impossible to state whether this organism is an opportunist, making the most of unusual environmental conditions, or whether it is the primary offender. Gonorrheal vaginitis, rarely occurring during this time, may be ruled out by the Gram stain method.

#### PRESENT DATA

The patients in this series all had an artificial or spontaneous menopause. They all complained of the characteristic symptoms of senile vaginitis, which was confirmed on examination. Many of them had been patients in our own clinic for several months and their condition had failed to respond to the usual therapy. Some of them had been treated elsewhere at various times, with little or no improvement. In each instance a biopsy specimen was taken from the vagina before treatment was instituted with repeated biopsies

every 3 weeks for a period of 4 or 5 months. Biopsies of the vagina can be removed without pain by the injection of a small amount of novocain locally according to the method described in a previous communication. All other treatment was discontinued. In some instances it was difficult to persuade the patient to refrain from taking vaginal douches containing various medications which they had used for years.

The cases were divided into several groups, according to the type of treatment. The largest group received 100 rat units of ammonium (Squibb) subcutaneously three times weekly. In addition to this, a vaginal suppository containing 75 rat units of ammonium was used each night. The duration of the treatment averaged 6 weeks, although in most instances the symptoms disappeared after the first 10 days. A second group of patients received only subcutaneous injections of 100 rat units of ammonium. This was done to eliminate the





Fig. 4. a, The squamous epithelium before treatment.  
b, Three weeks after treatment. Note the marked increase in the thickness of the squamous epithelium. The basal layer consists of three or four rows of actively growing cells. A dense functional is developing.  
(All photomicrographs were magnified 425 times for accurate comparison of the squamous epithelium.)

Examination on November 23, 1934, revealed normal appearing mucosa. The patient had no complaints. A fourth biopsy as taken and amniotic treatment continued (Fig. 4d).

On December 4, 1934, fifth biopsy was taken. The mucosa appeared normal and the patient's condition was improved. Since this time she has used three or four vaginal suppositories weekly for 6 weeks. The vaginal mucosa has retained its normal healthy condition and she is apparently entirely cured.

CASE 3. Van E. Unit N. 8572, aged 65 years, as first seen on June 29, 1934, complaining of marked burning and discomfort in the vagina and on urination. Local treatment was of no avail and the symptoms became steadily worse. The patient had normal menopause 20 years ago.

On examination, the vagina was found to be severely but constricted and shortened. The vaginal mucosa was thin, shiny, and yellowish in color, except for many small superficial hemorrhagic areas. A biopsy was taken and the patient was given 100 ml units of amniotic intramuscularly four times weekly (Fig. 3, a).

A second biopsy was taken on July 27, 1934 (Fig. 3, b). At this time the mucosa had regained some of its normal elasticity, appeared smooth, and no petechial hemorrhages were present. The patient volunteered that she was feeling better than she had in years. The treatment was discontinued for 4 weeks, after which she again returned. On examination considerable regression of the improvement and few petechial hemorrhages were noted, although the patient had no complaints. Amniotic treatments were again instituted and continued for 6 weeks.

The third biopsy as taken on November 3, 1934 (Fig. 3, c). The patient's condition was markedly improved. She has been symptom free since the last course of treatment.

CASE 4. A. P. Unit N. 86, aged 48 years, as first seen on September 7, 1934, complaining of an offensive, irritating, vaginal discharge, dyspareunia, burning on urination, and pelvic discomfort. Local applications of various drugs and douches gave no relief and the condition grew progressively worse. Radiation treatments for fibrosarcoma were given 16 years ago, which produced an artificial menopause.

On vaginal examination the mucosa, particularly at the introitus, as found to be inflamed and glistening. Multiple petechial hemorrhages and superficial ulcers were present. A biopsy was taken and 100 ml units of amniotic were given hypodermically three times each week and one respiratory supply (Fig. 4, a).

On October 2, 1934, the patient noted that she felt better than she had in years. The mucosa appeared entirely normal. A second biopsy as taken and amniotic treatments continued (Fig. 4, b).

The patient returned for examination on November 3, 1934, and had no complaints. The mucosa was normal in appearance. Further treatments were discontinued.

CASE 5. L. G. Unit N. 8606, aged 40 years, as first seen on November 1934, complaining of profuse, vaginal discharge for the past 3 months. She had spontaneous menopause 3 years ago. There was generalized inflammation of the introitus and the vagina, so that examination was painful. Speculum examination showed the vaginal mucosa to be smooth, glistening, and atrophic. Hanging drop examination of the discharge was positive for Trichomonas vaginalis. Local treatment gave only temporary relief and the discomfort, burning, and vaginal discharge continued.

A biopsy was taken on October 3, 1934, and 100 ml units of amniotic were given hypodermically three times per week. Vaginal suppositories were ordered nightly (Fig. 3, c).

A second biopsy was taken on October 24, 1934 (Fig. 3, b). The patient's condition showed marked improvement. Hanging drop examination was negative for Trichomonas. After 6 weeks, the treatment was discontinued and the patient has had no complaints to date.

#### EVALUATION OF STUDY

The vaginal mucosa is under the influence of the ovaries. Cyclical changes in the monkey have been described in a previous communication. Similar cyclical changes dependent on ovarian activity in the human female have been reported by Papanicolaou. This cyclical activity dis-



Fig 5 a, Note the small compact cells of the atrophic squamous epithelium and the moderate infiltration of round cells in the subepithelial zone  
 b, Three weeks after treatment Note the orderly arrangement of the basal cells, the large clear cells of the basalis, and the development of the functionalis. The inflammatory cells and subepithelial connective tissue have disappeared  
 (All photomicrographs were magnified 425 times for accurate comparison of the squamous epithelium)

pears following the menopause and the mucosa slowly atrophies so that it consists of only several layers of inactive cells. Allen castrated monkeys and followed these retrogressive changes in the vaginal mucosa. In our study, we were able to rebuild the atrophic vaginal mucosa in a monkey castrated over a year in 2 weeks' time with estrogenic hormone. Dierks recently reported that he produced a good functional layer in the vaginal mucosa of a castrated young woman with very large doses of estrogenic substance.

The theory upon which the present treatment was commenced was that the changes in senile vaginitis would disappear if the mucosa could be restored to the type present during active sex life. This would lead to the healing of the superficial ulcerations in the mucosa, the rapid disappearance of inflammatory changes, and the subsequent cessation of adhesive processes. The amount of estrogenic substance necessary could be determined only by careful study of the patients and repeated histological examination of the mucosa. The small amount of estrogenic substance required for a complete restoration of the normal mucosa and the rapidity of action was a distinct surprise. The marked responses of the atrophic epithelium to the dosage used made the present therapy easy and entirely feasible.

The changes in the vaginal mucosa as a result of treatment with estrogenic substance are indeed interesting. The inactive basal cells rapidly begin to proliferate and abundant mitoses can be seen in them. The number of cells in the basalis rapidly increases. They exhibit all the signs of active growth. Under continued stimulation the basalis

develops a good functional layer and the typical zone of intra-epithelial cornification can be seen. The cells soon contain an abundance of glycogen.<sup>1</sup> The inflammatory foci beneath the squamous epithelium usually seen in senile vaginitis disappear. A marked increase in the vascularity of the submucosa likewise occurs. All of these striking changes can be followed accurately in the photomicrographs which are all of the same magnification, so that proper comparisons may be made.

The patients show improvement within a few days after treatment, and in most instances their symptoms have all disappeared in about 10 days. A general feeling of well-being is usually present and some of the elderly women insist that they feel better than they have in years. Grossly, the changes are quite apparent. The mucosa becomes somewhat velvety, more elastic and more distensible. All signs of inflammation and irritation disappear. Petechial hemorrhages, superficial ulcerations, and filmy adhesions likewise disappear and the discharge stops.

These changes, however, are not permanent. Several weeks after the cessation of treatment, the mucosa rapidly returns to its previous atrophic condition. Within 4 to 6 weeks the usual senile mucosa is again present. However, the patient's symptoms do not return, unless she has not received enough treatments and some inflammation still remains. If she has been treated for a sufficiently long time so that the mucosa has healed completely and all subepithelial inflammation has disappeared, then the symptoms do not return.

<sup>1</sup> A complete histological study of the glycogen changes in the vaginal epithelium upon which the hydrogen ion concentration and bacterial flora depend will be reported later.



until those factors which produce senile vaginitis again are present. If trauma and infection are again introduced, senile vaginitis will undoubtedly recur. In our series it was found that the patients should be treated for a period of 4 to 6 weeks. The patients with marked changes should be treated for 6 to 8 weeks. In all of our cases the results were good; the symptoms all disappeared and remained cleared up for at least 6 months, during which time the patients were carefully followed. This sequence of events demonstrates conclusively that the physiological changes in the vaginal mucosa in themselves do not produce symptoms. If trauma and infection are introduced, senile vaginitis develops.

In some of our cases the patients were treated for *Trichomonas vaginitis* for a considerable length of time. These were the most stubborn and difficult cases because they did not respond to the usual therapy for this condition. A few of these cases were treated with estrogenic substance and to our surprise they cleared up rather promptly. Undoubtedly the difficulty in eradicating the infection was due to the fact that the mucosa was so atrophic. A restoration of the mucosa to the normal adult type seen during active sex life caused a prompt disappearance of the organisms. It is likely that the organism itself was only an accidental finding and may have played little or no role in the causation of the symptoms. It is therefore suggested that in the treatment of *Trichomonas vaginalis* vaginitis occurring in the postmenopausal period an estrogenic substance should be used as an aid to whatever therapy is desired.

#### SUMMARY

The treatment of senile vaginitis heretofore has been extremely unsatisfactory. The use of an

estrogenic substance amnioin (Squibb) rapidly restores the normal adult epithelium seen during active sex life. The simple restoration of the epithelium leads to a healing of the ulcerated areas, a disappearance of the inflammatory symptoms, a cessation of the adhesive manifestation, and a complete disappearance of all symptoms. Undesirable effects have been noted nor can they occur during the postmenopausal period. Although the vaginal mucosa reverts to the normal senile type the symptoms do not recur. Interesting biopsy specimens showing all the changes initiated by the estrogenic substance in the vaginal mucosa are presented. The treatment is simple, inexpensive and entirely feasible. The biopsy method of study can be used as an aid in all endocrine studies in the human female.

I wish gratefully to acknowledge the co-operation of Dr. J. J. Durrant and Dr. J. A. Marrell of E. R. Squibb and Sons, and the liberal supply of amnioin which they furnished for this study.

#### REFERENCES

- ALLRED, EDNA. The Menstrual Cycle of the Menopausal Women. *Obstetrics and Gynecology* 10, 98, Carle Hospital, Urbana, Ill., 1934, pp. 1-144.
- DAVIS, M. EDWARD, and HART, V. CARL G. Changes in vaginal epithelium during pregnancy in relation to the vaginal cycle. *J. Am. Med. Ass.* 1935, 104, 579.
- DREXLER, K. Normal monthly cycle of human vaginal mucosa. *Arch. f. Gynaek.* 1931, 90, 30.
- ELDER, EUGENE. Experimental *Urethrovaginitis* as a mechanism of vaginal infection. *Arch. f. Gynaek.* 1929, 86.
- LEWIS, ROBERT M. Study of effects of theelin on human vaginal vaginitis in children. *Am. J. Obst. & Gynec.* 1933, 26, 593.
- PAPANICOLAOU, G. N. Sexual cycle in human female as revealed by vaginal smears. *Am. J. Anat.* (suppl.), 1933, 67, 60.
- IDEAN. Diagnosis of early human pregnancy by the vaginal smear method. *Proc. Soc. Exper. Biol. & Med.* 1935, 32, 436.

## FERRIC CHLORIDE COAGULATION IN TREATMENT OF BURNS

## WITH RESUME OF TANNIC ACID TREATMENT

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THE record of ten years of treatment of burns by coagulants has firmly established the principles enunciated by Davidson (5), when he introduced tannic acid as an external application in 1925. The work recorded here was stimulated by the success of his treatment, together with the belief that some other preparation might be found better than tannic acid.

Davidson (6, 7, 8) attacked the problem in the field of physiology, pathology, and biochemistry, consolidated the experimental work of others, added many observations of his own, and evolved a completely rational outline of burn treatment for the first time in medical history. It may well be said that his work bears the same relation to modern management of burns, as that of Lister to modern surgery. In that connection it will be recalled that the surgical principles, demonstrated by Lister, have perpetuated his memory long after phenol sprays and solutions disappeared from operating rooms. In a similar way, Davidson will be remembered because of his declaration of the principles of coagulation treatment, even though tannic acid may be displaced by other materials as an external application. In other words, tannic acid, itself, seems to be a comparatively minor factor in the so-called "tannic acid treatment."

We recognize a marked reduction in mortality and morbidity since the popularization of primary coagulation. Beck and Powers, Seeger, Glover, and Wells have contributed valuable suggestions in modifying the original technique. The work of Penberthy and Weller, especially in the surgical treatment of late complications, makes possible the rehabilitation of many apparently hopeless cases. Beekman noted a mortality percentage almost cut in half. From other countries, notably England (23) and Austria (24) come reports of decreased mortality and morbidity in recent years. McClure and Allen (13) have recently presented convincing statistics, establishing the value of tannic acid.

Davidson summarized the advantages of the tannic acid regimen as follows: (1) it lessens toxemia, (2) is analgesic, (3) minimizes trauma, (4) conserves body fluids, (5) limits secondary infection and consequent scar formation, and (6) forms scaffold for growth of young epithelial cells.

Each statement remains unchallenged after years of clinical trial.

## OBJECTIONS TO TANNIC ACID

1 *Instability of solutions* Glover (9) called attention to the rapid oxidation of tannic acid to the darker, more irritating gallic acid, after a few days' exposure to light and air. The preparation of fresh solutions seems imperative, the marketing of prepared jellies, and the storage of stock solutions in hospitals and physicians' offices seem equally illogical.

2 *Stiffness of coagulum* This may cause too early splitting, or loosening at the edges, with defeat of the main purposes of coagulation. In the region of a joint, early mobilization may be prevented, and functional recovery thereby retarded, or the patient's conscious or unconscious movements may loosen the eschar too early, with resultant infection and excessive scarring. Lock (11) warned against the use of tannic acid around the circumference of a finger, because of the danger of gangrene after the digit swells.

3 *Necrosis and infection under coagulum* Aldrich remarked that it is difficult to discover infection under a tannic eschar until it is very extensive. In my experience infection tended to burrow and spread under tannic coagulum rather than localize.

4 *The time factor* This affects results in two ways. In the first place, a material which can be depended upon to coagulate more rapidly, would erect a more dependable barrier against infection. In the second place, where the average tannic eschar requires removal in 2 weeks or less, a coagulum which could be depended upon to hold for a longer period, would give the new epithelial cells more time to consolidate the reparative process, especially in third degree burns. It follows logically that in many cases, skin-grafting might thereby be avoided.

## USE OF OTHER COAGULANTS

Seeger claimed improved results by neutralizing tannic acid solutions with sodium carbonate to approximate a hydrogen-ion concentration of 7.0. He has also worked in conjunction with chemists in the tanning industry, on other coagulants in the tannin group. Aldrich has used gentian violet and other dyes, which coagulate proteins slowly.



Fig. 1. Case. Leg, showing extent of voluntary section of knee. Left, note crackling of coagulum on fifteenth day. Right, the epithelialization on twenty-fourth day. The dark areas at the right were injured by too early removal of coagulum, and re-coagulated with mercuric iodine.



Fig. 2. Case. Hand showing appearance of coagulum on fifteenth day and after its removal on twenty-fourth day.

strengthen their value as antiseptics. Shillito suggested silver nitrate solutions, ionized by exposure to ultra violet light. I tried this method once, obtaining a very hard coagulum, with a good end-result in a small third degree burn. Bettman recently urged the use of 10 per cent solution of silver nitrate, following tannic acid claiming a more flexible coagulum, and more rapid coagulation. Stummel commented on the use of gallotannate of iron (black ink) by Hippocrates for at least two or three generations he remarked about surprising recoveries in cases observed by him.

#### FERRIC CHLORIDE—RATIONALE

My interest in ferric chloride was aroused by a case encountered in 1929, a man burned by immersion in a vat of actively boiling ferric chloride solution. The impressive features of the case were (1) primary coagulation by the chemical itself without any other external treatment (2) flexibility of the coagulum, permitting fair motion of all joints (3) comfort of the patient in spite of deep extensive involvement of both legs up to the mid-thigh level and (4) an excellent end result, with 100 per cent functional recovery in 3 months, in spite of the fact that I was timely removed the coagula much too early.

No animal experimentation was attempted, because of the dissimilarity in the reaction of hairy

animals, as compared with burned human skin. More recently a few comparative observations have been made by applying various coagulants to the areas from which skin-grafts have been taken, studying the effect of different agents on the same individual. Proceeding cautiously first only with minor burns, later with those of greater extent and depth, a series of over 40 cases was observed with several physicians.

Some precedent for the use of ferric chloride was found in the literature. I had seen the remarkable relief and rapid recovery of patients from dermatitis venenata (ivy poisoning) under ferric chloride treatment, as proposed and rationalized by McHaur. Slack had reported the use of tincture of ferric chloride on burns as far back as 1891 and John B. Murphy had commented favorably on the treatment. There was no evidence that anyone had given the preparation intensive study or extensive trial, probably because the advantages of coagulant treatment were not recognized prior to Davidson's work.

Slack claimed the following merits for ferric chloride: (1) it relieves pain promptly in 5 minutes, (2) forms a dry surface requiring no dressings, (3) prevents infection, (4) heals quickly with little scar formation, and (5) is convenient, inexpensive and easily applied. He failed to express the biochemical concepts, as did Davidson, but otherwise the similarity of their findings is striking.

#### CHEMISTRY AND PHARMACOLOGY

The U. S. P. solution and tincture of ferric chloride contain an excess of hydrochloric acid, which

is considered objectionable. By addition of increasing amounts of sodium hydroxide, a reaction occurs, represented by the formula  $\text{FeCl}_3 + 3\text{NaOH} = \text{Fe}(\text{OH})_3 + 3\text{NaCl}$ , or intermediate stages by varying proportions of ferric chloride and ferric hydroxide, the latter being very soluble and fairly stable in solutions of the former. This makes possible a choice of solutions of variable hydrogen-ion concentration, ranging from 3.2 to 6.9, according to estimations made so far. After a week or two there may be some precipitation, but the supernatant liquid remains quite effective as a coagulant, and is less irritating than the fresh solution.

The transition from ferric chloride to the hydroxide, with the intervening theoretical compounds, and the dialysis of the colloidal hydroxide sol, form a fascinating chemical study, which need not concern us here, except to note that the hydroxide coagulates proteins, and solutions of ferric hydroxide in the chloride are just as effective as the chloride alone. Lund and Wuefelfert and Lindau have presented experimental data, measuring the coagulant effect of dialyzed ferric hydroxide sol.

Dialyzed iron (representing 5%  $\text{Fe}_2\text{O}_3$ ) has been used in five relatively minor burn cases, with promising results. Coagulation is slower than with ferric chloride, but more rapid than with tannic acid. I believe it is the least painful coagulant that I ever used. Further observation is necessary before recommending its general use.

In most of the cases treated so far, we have used 5 per cent aqueous solutions, made by dissolving commercial anhydrous ferric chloride in distilled water, and filtering. This has been alkalinized in some cases by addition of sodium hydroxide. Solution of ferric chloride in glycerin has been used in 2 cases, but is not recommended. Our experience with tragacanth jelly has been too meager to draw any conclusions. The following solutions are useful, because they can be obtained easily at any pharmacy:

- |   |      |
|---|------|
| (1) R Tincturae ferri chloridi            | 30 0 |
| Sig. Paint over small, unbroken blebs     |      |
| (2) R Tincturae ferri chloridi            | 15 0 |
| Sodu hydroxidi                            | 0 3  |
| Aque destillatæ q s ad                    | 30 0 |
| Sig. Paint or spray over denuded surfaces |      |

#### TECHNIQUE

In technique of application, there is no essential difference between tannic acid and ferric chloride solutions. A pledget of cotton on a wooden applicator is sufficient to cover a small area. In more diffuse burns atomizers are preferred, my

personal choice being a cheap metal type, such as those sold with insecticides, their low cost permitting rejection after use in one or two cases.

The primary pain of ferric chloride coagulation may be considerable, about the same as that noted in the use of tannic acid, but after 5 minutes there is the same secondary analgesic effect. Morphine or barbiturate analgesia is desirable, and in some instances nitrous oxide anesthesia, or preliminary local applications of butyn or nupercaine solutions may be preferable.

Potentially infected burns, in which coagulation has been delayed over 6 hours, have usually been prepared by preliminary sponging with gauze, moistened in sodium hypochlorite solution, which serves for both antiseptics and débridement. Clean burns, seen before meddlesome self-treatment, have been treated by aseptic débridement, and immediate coagulation of denuded surfaces. First degree burns, and those of second degree, showing only small, unbroken blebs, are simply painted with tincture of ferric chloride every 2 hours, with no dressing, later coagulation may or may not be necessary.

A coagulum should be left intact until it can be removed without exposing any bleeding surface, but any loosened portion should be cut away as a possible focus of infection. Then it may be desirable to apply some antiseptic, as a secondary coagulant, such as gentian violet, or an acetone-alcohol solution of metaphen or mercurochrome.

With an average second degree burn, the eschars may be removed with a dry underlying surface in 12 to 14 days, however, in several cases the coagula have been left undisturbed for over 3 weeks, with evident benefit from the prolonged protection of the healing surface.

Skin-grafting should be considered, if any wide, unhealed areas remain a week or 10 days after removal of the coagulum. Fortunately, it has not been indicated in any of our cases so far.

#### CASE RECORDS

A few cases are presented, illustrating a variety of problems, including the only fatal case in our series. The only cases not reported, in which ferric coagulation was not entirely successful, were small, infected burns, seen over 3 days after injury, where active infection contra-indicated the use of any coagulant. In such cases moist dressings (Dakin solution preferred) are probably the best solution of a difficult problem. Ointments have practically no place in burn treatment, infection is the inevitable result. The one exception to that rule has been superficial facial burns, treated with butesin picrate ointment.

**CASE 4.** A male laborer, aged 33 years, was admitted with second and third degree burns of entire dorsal surface of left hand, including all fingers, and entire circumference of left leg, including knee and popliteal space caused by throwing pall of tallow on an open fire (Figs. 1 and 2). Deficient with wet gauze (Dakin solution) as followed by spray of 5 per cent aqueous solution of ferric chloride every hour for three applications. Eighteen hours later

few new blisters and the edges of the burns were treated in the same manner. By that time firm, flexible, anolog any-brown coagulum had formed. Six days later after edema had subsided, these had become wrinkled, as shown in photographs, but still remained firm. Mobilization of all joints was urged from the eighth day but the fingers could not be moved much until the fourth week. About 75 per cent of the coagulum was loose enough to be removed on the fifteenth day; that over the deeper burns was left until the twenty third day. The entire surface was free from infection, excepting small, walled-off pocket centimeters in diameter over the third metacarpophalangeal joint. He was walking about the ward on the twenty-fourth day and left the hospital on the thirty-first day. The patient removed five loose, charred fragments on the date of discharge. The leg was considered normal on the fortieth day with completely restored function of the hands and fingers after ten days, at which time he returned to his usual work (Dr. J. G. Knapp).

**CASE 5.** A woman 8 months pregnant, aged 30 years, was burned by an explosion of naptha while cleaning clothing, the entire body surface being involved, except the scalp and the soles of the feet. Gentle debridement with wet gauze was followed by spraying with 5 per cent aqueous solution of ferric chloride. A good, flexible coagulum was obtained, and the patient was remarkably comfortable after the first hours. A stillborn fetus was delivered 48 hours after edema collapse ensuing, with death 3 hours after delivery. Mentally alert and rational until after delivery this case is an example of complication of burning case, providing maximum comfort following an inevitably fatal burn (Dr. E. H. Engel).

**CASE 6.** A man aged 30, husband of patient, Case suffered second and third degree burns of the entire surface of both hands and wrists, incurred in his effort to extinguish the fire. Good coagulation was obtained 8 hours after the first application of ferric chloride. His mental condition was agitated during the first few days, incident to the shock of the accident and his wife's death, with a background suggesting an acute alcoholic psychosis. His maximum temperature was 101° degrees F. with recession to normal on the fifth day when he was transferred to another hospital. There his coagula were forcibly removed under ether anesthesia on the fourteenth day, the propriety of this procedure being questionable. He returned under our observation 4 days later with small coagulating crusts on the flexor surfaces of the fingers. On the twenty-sixth day these had healed, and function of the hand was estimated over 90 per cent. On the thirty-fifth day function was 100 per cent, and he was piloting an aeroplane.

**CASE 7.** A 3 year old boy was rescued by firemen from burning shed, where there appeared to have been an explosion of oil of turpentine, causing deep second degree burns of the dorsal surfaces of both hands, all fingers, neck, left cheek, both ears, nose, forehead, and scalp. The child was taken to the hospital, but was removed by his father and treated at home with one of the many pernicious proprietary antiseptics. When seen on the third day the bandaged areas were discharging, new blisters were filled with purulent fluid, and lesions of impetigo contagiosa were appearing on his leg and abdomen. Two brothers were found to have scapitula. His temperature was 102.6

degrees F, but plans for hospitalization were underway. Under barbaric antiseptic, antiseptic debridement with disinfected gauze, and coagulation. His 5 per cent solution of ferric chloride in 90 per cent alcohol was carried out over all burned areas, except the scalp. Good coagula formed in about half hour. After clipping the hair, center of amputated nuchary was entered for the scalp and the impetigo lesions. I was pleasantly surprised by the course of the burns. The temperature was never found above 101 degrees F. the child appeared to be comfortable, and the coagula held remarkably well. From the seventh to tenth day portions of the crusts were trimmed away from the left hand, neck, and forehead, because of infection beneath, and secondary coagulation with alcohol acetone solution of metaphase was done. Over two-thirds of the involved area healed without evidence of infection. The only appreciable scar was about centimeter in diameter on the forehead close to the hair line. On the seventeenth day the last coagula were removed. The temperature had been normal after the eleventh day, and recovery was considered complete on the twenty-fifth day. Amputation was noted only on the day following coagulation. This was particularly trying case, and admitting the element of good fortune, the result as far better than the usual expectation.

**CASE 8.** A male laboratory technician, was burned by explosion of flask, containing an inflammable solution of phenol and trimethyl carbol,  $(CH_3)_3COH$ , his entire back being burned from the scapula to the level of the iliac crests. The phenol presented an element of danger fatal cases having been reported due to absorption through burned skin. Within half hour 5 per cent alcoholic solution of ferric chloride was applied to the burned area.

black, oily stabs, suggesting the presence of phenol, appeared at once. At the hospital 8 hours later debridement and coagulation were done, the denuded area covering about 1,500 square centimeters. On the third day the temperature reached 104 degrees F. the patient was anemic, and albumin and casts were found in the urine. About 80 per cent of the burned area required reoperation on the fifth day, probably because it was impossible to keep the patient from moving about, and lying on his back. The temperature and urinalysis were normal after the eighth day; the coagula loosened on the tenth to thirteenth day recovery was considered complete on the twenty-fourth day when he returned to work. Later examination indicated that his acute nephritis had cleared completely (Dr. J. G. Knapp).

It is noteworthy that in the chemical industry tincture of ferric chloride is considered a better antidote in phenol burns than alcohol alone. A blue-black, inky non-toxic iron salt, possibly a tannate being formed.

**CASE 9.** A chemist, aged 30 years, was burned about the head and forehead, involving both the wrist and elbow by splash of liquid anhydrous ammonia from broken flask. It was treated primarily by application of tincture of ferric chloride to the unbroken skin every hours. After 48 hours several large blisters were opened, and the denuded surfaces, approximating 550 square centimeters were coagulated with the 5 per cent aqueous solution. This was complete in half hour. His maximum temperature was 100 degrees F. he was comfortable, with good motion of involved joints, and returned to light work of his own volition after 7 days. The coagula were allowed to loosen spontaneously this occurring in from 14 to 20 days. Recovery was complete by the time this was finished.

**CASE 7** A moulder, 50 years old, suffered second and third degree burns from a splash of molten brass, involving the left middle finger, wrist, dorsal surface of left forearm, elbow, and lower third of upper arm. He was first seen 18 hours after the accident. Because of the delay in treatment, a moist dressing (Dakin solution) was applied for an hour before coagulation, which was done with 5 per cent aqueous solution of ferric chloride. Coagula were firm, flexible, and tenacious, with free motion of involved joints. There was no appreciable rise of temperature, and healing was complete upon removal of loose eschars between the ninth and eighteenth day, according to the depth of the burns. He was at work on his usual job on the twenty-sixth day.

**CASE 8** A male laborer, aged 26 years, was scalded by boiling water, causing second degree burns of the dorsal surfaces of the toes and left foot, ankle and leg up to the knee. This was treated 6 hours after the accident by aseptic débridement, followed by application of a 2 year old solution of ferric chloride (5 per cent aqueous), with similar treatment of new blebs and edges of burns after 24 hours. Coagulation was complete after 2 hours, the maximum temperature was 99 degrees F, there was no discomfort after the first night. The patient left the hospital on the fourth day, and was walking about the house on the seventh day, without permission. The coagulum was firm, but pliable, wrinkling to adjust itself to movement of the ankle in walking. It was removed easily on the fourteenth day, with healing complete except for one small area (2 by 3 centimeters) which bled. That was my error, only loose coagula should be removed. There was no evidence of infection at any time, and the patient returned to work on the twenty-ninth day.

**CASE 9** A male infant, 13 months old, was scalded by overturning a kettle of boiling water. Two relatively superficial second degree burns of the abdomen and right thigh (240 square centimeters) were coagulated by bandaging for 12 hours with 5 per cent tannic acid jelly. Denuded areas on the penis, scrotum, left thigh, knee, leg, ankle, foot, and toes were immediately coagulated by ferric chloride, two applications of the aqueous solution being required an hour apart. The ferric treated area approximated 1,200 square centimeters. The maximum temperature was 101.4 degrees F, with no fever after the fourth day. From the second day, when a few new blebs were opened for coagulation, until the ninth day, no local treatment or any sedative was necessary. Then tannic coagula, and the ferric eschars over a similar burn on the left thigh were removed, showing dry epithelialized surfaces underneath. The more deeply burned areas on the foot and leg were exposed between the fourteenth and nineteenth day. All surfaces were dry with no crusts or scarring, excepting a keloid-covered area 3 centimeters in diameter, found on his ankle 6 months later. Recovery was considered complete on the twenty-third day. In this case the tannic jelly gave an excellent result, but ferric chloride, given a much more severe test, showed equally good results, with more flexible coagula.

**CASE 10** A male laborer, aged 26 years, was also scalded by boiling water. Five per cent solution of tannic acid was applied to a denuded surface (250 square centimeters) on the outer aspect of the right thigh, while 5 per cent aqueous solution of ferric chloride was used on a similar area on the right arm and forearm, involving the elbow. The ferric coagulation was complete within an hour after two applications, that with tannic acid required eight applications over a period of 24 hours. Subjectively, the pain of each application was reported about the same, with the advantage in favor of ferric chloride, because coagulation was more rapid. The ferric coagulum was

flexible enough to permit fair motion of the elbow, with crinkling over the arm as the edema subsided, and the joint was moved, but without loosening until healing was complete. On the seventh day the tannic coagulum had split horizontally, and was loose at the edges. Both were removed on the fifteenth day, with equally excellent end-result. As a single instance, with ferric chloride given the more severe test, it was more satisfactory than tannic acid.

#### EVALUATION OF RESULTS

In general, where the burn is not deep, and does not involve an area about a joint, when coagulation is done promptly, with slight possibility of infection, there is little or no difference in the relative merit of tannic acid and ferric chloride solutions. However, the following comparisons are indicated by the observations so far.

**1 Stability of solutions** Tannic solutions become irritating in a short time, those of ferric chloride precipitate basic iron salts slowly, but the solution remains effective and rather less irritating. (In Case 8, a 2 year old solution was quite effective.)

**2 Consistency of coagulum** That of tannic acid has been likened to sole leather, that of ferric chloride to top leather, of varying thickness, according to the depth of the burn. Early mobilization of joints is usually possible without disturbing a ferric coagulum, in my experience, this has not been possible with tannic acid.

**3 Necrosis and infection** These complications are considered jointly, because both are invariably present when either occurs. The principal difference is that with ferric chloride, infected or necrotic areas have been small, localized lesions, rather easily detected by palpation, while under tannic coagula, I have been able to discover them only after burrowing and spreading, and draining at the edge.

**4 Staining of skin** This deserves consideration because Pusey has reported brown stains of the skin after the use of wet dressings of ferrous sulphate solution, and electric burns in the presence of iron have been known to leave a brownish-black deposit in the skin (25). Among 52 traced cases, the only stain noted followed a phenol burn, presented a light-brown freckled appearance. Since phenol burns are prone to leave stains (brown, reddish brown, or purplish, 25) the use of ferric chloride was not considered the cause of the stain. At first we hesitated to use it on the face, but more recently it has been applied to the face, forehead, and eyelids. The chemical, of course, is removed with the coagulum. The solution is easily removed from the hands by rinsing in clear water, or a weak acetic or citric acid solution.

5 *Staining of linen* Hospital executives have complained because iron stains are not removed in ordinary laundering. The best decolorizing agent is a solution of potassium fluoride with an excess of hydrofluoric acid after decolorizing the spots, clear water is used for rinsing; the fluoride solution should not be used on the hands. This solution is available at any laundry supply house.

6 *Tenacity of coagulum* Ferric coagula have been removed in good condition as late as the twenty third day, serviceable tannic coagula are seldom seen after the fifteenth day. With ferric chloride we see wrinkling of the coagulum with movement of joints, and after swelling subsides, without any loosening. In my opinion, this is the greatest advantage of ferric chloride over tannic acid.

#### SUMMARY

1 Solutions of ferric chloride used to coagulate burns show the same advantages as tannic acid, with certain definite points of superiority, especially in providing for early mobilization of joints.

2 Further clinical work with ferric salts is desirable. More extensive study of the hydrogen-ion concentration values of the various chloride hydride solutions is planned, also further investigation of the clinical possibilities of colloidal ferric hydride alone and in solution with ferric chloride.

3 The general condition of the burned individual transcends in importance the choice of external application. However early coagulation of denuded surfaces must be regarded as an important factor in treatment, and an essential factor in achieving the best results in diffuse burns.

#### REFERENCES

- ALDRICH, R. H. The role of infection in burns. *New England M. J.* 911, 208-209.
- BECK, C. S., and POWERS, J. H. Burns treated by tannic acid. *Ann Surg.* 90, 24, 9.
- BERMAN, F. Tannic acid treatment of burns. *Arch Surg.* 90, 18-20.
- BUTTRICK, A. G. Tannic acid silver nitrate treatment of burns. *Northwest Med.* 935, 34-37.
- D. VIGOR, E. C. The use of tannic acid in the treatment of burns. *Surg. Gynec. & Obst.* 1923, 4, 202.
- Idem. The prevention of toxicemia in burns. *Am J Surg.* 90, 40-41.
- Idem. Sodium chloride acetabulum in cutaneous burns. *Arch Surg.* 93, 3-10.
- DAVIDSON, E. C. and MATTHEW, C. H. Protein proteolysis in cutaneous burns. *Arch Surg.* 1927, 5, 205.
- GROVER, D. M. Six years of tannic acid treatment of burns. *Surg. Gynec. & Obst.* 1911, 51, 921.
- LEONARD, G. Ueber die Extraktion von Extraktstoffen aus Elektrohydrolysat. *Biochem. Zeitschr.* 93, 219-225.
- LOCK, V. Treatment of burns. *Clin J.* 911, 6-100.
- LOTT, G. and W. KISSER, K. Ueber die Fäulnis von Elektrolysen und Elektrohydrolysat. *Biochem. Zeitschr.* 93, 9-7.
- McCLURE, R. D. and ALLAN, C. I. Davidson tannic acid treatment of burns (ten year results). *Am J Surg.* 1925, 28, 370.
- McNANE, J. B. Contribution to chemotherapy of skin dermatitis and tentative method of treatment. *Arch Dermat. & Syph.* 931, 3-10.
- MORRIS, J. B. *Practical Medicine Series*, 912, 161-164.
- PERKINS, G. C. and WALLER, C. A. Complications associated with the treatment of burns. *Am J Surg.* 934, 20-24.
- PRATT, H. A. Stabwunden. *J. Am. M. Ass.* 1917, 78, 637.
- SCHERER, S. J. The hydrogen ion concentration value of tannic acid solutions used in the treatment of burns. *Surg. Gynec. & Obst.* 934, 33-35.
- SENAZAR, L. Iodized silver in treatment of burns. *Brit M. J.* 929, 663.
- SLACK, H. R. New treatment of burns. *J. M. Ass. Georgia*, 9, 4, 51.
- STANBACH, C. A. Fungic use of ink in burns. *J. Am. M. Ass.* 929, 1-4.
- WALLER, D. B. The aseptic tannic acid treatment of diffuse superficial burns. *J. Am. M. Ass.* 923, 10-15.
- WILSON, W. C. The tannic acid treatment of burns. *Sp. Rep. Series*, 14. Privy Council, Medical Research Council, H. M. Stationery Office, London, 1920.
- Various Letters. *J. Am. M. Ass.* 934, 91-93.
- Burns of skin with brown discoloration, (due to query). *J. Am. M. Ass.* 1920, 93 (197).

## MASSIVE RESECTION OF THE SMALL INTESTINE

## AN ANALYSIS OF 257 COLLECTED CASES

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FOR many years the term "extensive" when applied to resections of the small intestine has been indicative of the removal of lengths measuring 200 centimeters or more. This limit had been chosen early in the literature on resections, because it was estimated that such a length constituted approximately one-third of the small intestine, and represented, according to the experiments of Senn in 1888, the extent of the small bowel that might be removed from a given patient with safety.

It must be agreed that the surgical removal of large amounts of the intestine is not usually an elective procedure, for the surgeon is confronted at operation with the alternative of allowing the patient to die or resorting to a heroic effort to save the individual by resection.

## HISTORICAL

Perhaps the first massive resection of the small intestine was done by Koeberle in 1880 when he removed 205 centimeters. The patient recovered. Before 1900 additional cases had been reported by Obalinski, Fantino, Ruggeri, Shepherd, Schlatter, Dreesmann, Monprofit, and Franz. Collections of cases have been made by Schlatter (1906), Storp (1907), Soyesima (1911), Flint (1912), Flechtenmacher (1917), Cannaday (1919), Watson (1923), Brenizer (1929), and Dorow (1932). Dorow's case and his collection from the literature brought the total number of cases of massive resection of the small intestine to 97.

The present study consists of the reports of 3 cases and an analytical study of a total of 257 collected cases. In each instance, so far as was possible, the original reference was consulted. In reviewing the collected series of the various authors, a number of duplications have been eliminated in which the author of the article was other than the surgeon who performed the resection. A number of examples of shortcircuiting operations or exclusions of the small intestine as reported by Brohee, Ghedini, and Van Verts have been eliminated from the present study. Among his 83 cases, Brenizer has included Jackson's case of successful resection of 142 centimeters in a male infant of two, this is, undoubtedly, a massive resection of small intestine for a patient of such an age,

but it is not included in the present study. A number of collections have credited Kouwer with a resection of 224 centimeters, whereas this particular case was reported by Friele. One collector has included Boeckel's case in his series of extensive resections, but this is an error inasmuch as a review of the original reference shows there was a resection of 80 centimeters of ileum and 90 centimeters of colon.

The earlier collections have given the impression that there is a fairly high percentage of recovery, and that good functional results in extensive resection can be expected. They all have guarded the apparent good results with the statement that undoubtedly only the good results are apt to be reported in the medical literature. Flint recorded 48 recoveries in 59 cases, Flechtenmacher, 50 recoveries in 57 cases, and Cannaday noted 60 recoveries in 69 cases. Brenizer found a mortality of only 14.3 per cent in 83 cases with good functional results in 65.5 per cent of his series. Dorow reported a mortality of 18.6 per cent in his series of 97 cases.

## LENGTH OF THE SMALL INTESTINE

Inasmuch as the length of the small intestine varies with each individual, it must be remembered that a resection of a large amount in one individual would constitute a different percentage of the total length than in another, and if all other factors were equal, it is probable that different results might be obtained in 2 patients. The opinion expressed by the majority investigating intestinal lengths is that the length in the adult female is somewhat less than in the male. Some observers contend that negroes, Russians, and races living primarily on a coarse diet are inclined to have longer intestinal lengths. Lamb reported a negro with 1,216 centimeters (40 feet) of small intestine. Bryant found that the small intestine varied from 10 feet (304 cm) to 28 feet 4 inches (863 cm) with an average of 20 feet 6 inches (614 cm) in 160 adults. Beneke states there is a definite relationship between body length and intestinal length, and that for slender, average, and stocky individuals, there is an average of 389 centimeters of small intestine per 100 centimeters of body length. Wallenius is quoted by Kallio as having measured



the intestinal length in 212 Finnish patients and found an average of 760 centimeters. Kalso reviewed the reports of Meckel, Robson, Richter, Treves, Robinson, Tarnetsky, Drelle, Kubo, Chudinsky, Giacomini, and Wallentin. The reports mentioned when added to the 14 observations of Miyake and the 31 cases of the author's series in which the total small intestinal length was noted at operation or necropsy makes a grand total of 1162. These 1162 cases had an average intestinal length of 21 feet 6 inches (657 cm.)

#### CASE REPORTS

The 3 cases to be reported here include a careful metabolic study of the 1 case that survived operation.

**CASE 1. H. D. (A. M. B. H. N. 3540)** aged 4 years, white American male, truck driver, was crushed between two steel beams being lifted by steam cranes and the rear wheel of his truck. The main impact came on the left knee, and almost immediately the patient was unable to move because of severe abdominal pain. Less than 24 hours after the accident on May 14, 1930, the abdomen was opened by Dr. W. T. Harnack at the Illinois Central Hospital under ether anesthesia. The peritoneal cavity was distended with a large amount of fresh blood, the root of the mesentery of the entire ileum as far as torn at its abdominal attachment and was bleeding profusely. The bleeding points were caught and ligated. There are tears in the sigmoid and mesosigmoid and these were repaired. The ileum was raised well beyond the lines of demarcation of the disturbance of its blood supply from approximately the jejunal junction to about 8 centimeters short of the ileocecal junction. Because these two ends could not be approximated for an end-to-end anastomosis, the distal end of the jejunum was brought through a stab wound in the left rectum so as to establish fistula, and the end of the ileum was inverted. The abdomen was closed. The total length of the bowel measured within 4 hours after removal was 515 centimeters (16 feet 7 inches).

Immediately after operation, he was given 350 cubic centimeters of whole blood intravenously. On the third day after operation, drainage from the jejunal fistula stopped, but the soon discharged material again after the relief of an acute distention of the stomach. For the next weeks the patient received 60 to 5,375 cubic centimeters of physiological saline parenterally.

On May 3, under local anesthesia, lateral anastomosis was made between the jejunum and the middle of the transverse colon through a window in the omentum. The jejunal stoma was supposedly about 10 inches from the ileocecal end. The peritoneum was closed without drainage. The recovery from the second operation was rapid. The drainage from the fistula continued to be profuse, and all attempts to close the opening by means of stripping with adhesiv and packing the tract with gauze were unsuccessful.

On October 1, the jejunal fistula was closed, the post-operative course as entirely uneventful, and the wound was healed at the time of his discharge from the hospital on November 9, 1930.

On December 3, he was admitted to Billings Hospital for the service of Dr. L. R. Dragstedt for metabolic study. At the time of his admission he had lost 60 pounds since his operation 7 months before. His loss of strength was pro-

portionate with his loss of weight. Since the esophagus he had had an average of four yellowish watery stools daily. The day following his admission, further X-ray examination of the gastro-intestinal tract was carried out. Two hours after ingestion of barium, the head of the column was noted in the transverse colon, and at the end of 4 hours it had reached the rectum. Also, at the end of 4 hours, it was noted that most of the spaces meal was in the transverse colon and in a very dilated ileum. Twenty-four hours after the barium had been given, extreme dilatation of a loop of the ileum in the left side of the pelvis was noted.

The patient was discharged on February 8, 1931, after careful study had been made of his powers of assimilation. He weighed about the same at the time of his discharge as he had on admission to the hospital despite the fact there had been some discomfort in the number of daily stools on high carbohydrate, high protein, and low fat diet.

The patient was re-admitted to the Illinois Central Hospital on March 9, 1931, and died 4 days later of peritonitis. The history suggested that the condition had been present for about 2 weeks.

A necropsy was performed by Dr. H. G. Wells of the Department of Pathology, University of Chicago. The body was that of an emaciated man of 4. The most significant pathological findings were lesions to the gastro-intestinal tract. The jejunum was found to be anastomosed to the transverse colon 55 centimeters from the duodeno-jejunal junction. The jejunal mucosa of the first portion seemed normal. The blood end of the jejunum beyond the point of the anastomosis was also 55 centimeters long. Its contrast, as somewhat thicker than that in the upper segment. The terminal 30 centimeters of the ileum and was dilated to a diameter of 5 centimeters, and near the end of the stump were two fistulous openings into a pocket which apparently are the starting points of the perforations.

**CASE 2. P. R. (A. M. B. H. N. 55375)**, aged 36 years, housewife, was first seen in the Lying in Dispensary of the University of Chicago Clinics on March 2, 1931. She gave history of dull pain spreading gradually in the left upper quadrant on February 7, 1931, but she had no further distress until March 1. This attack was much more severe than the first, and it was accompanied by nausea and vomiting. After hospitalization, the patient's general condition became worse, nausea and vomiting were present along with abdominal pain and distention; and the leucocyte count amounted to 44,000 per cubic millimeter.

On the afternoon of March 24, 1931, the abdomen was explored by Dr. L. R. Dragstedt under nitrogen and ethylene anesthesia. The peritoneal cavity contained about 350 cubic centimeters of serous transudate. The entire small intestine was distended with gas and was discolored; the discoloration ranged from black to purple to dusky red. There was definite line of demarcation in the lower ileum, but this demarcation was not as clear cut in the upper portion of the small intestine. The entire ileum, except terminal few centimeters, and most of the jejunum were divided from peritoneal mesentery in one piece and the mass brought out through the lower end of the incision. After closure of the abdominal incision, Furr clamp was applied, and 460 centimeters of partly gangrenous intestine were removed.

The patient was given transfusion of 300 cubic centimeters of citrated blood and 700 cubic centimeters of saline immediately after operation. The next morning she felt fairly well, but at 9:30 a.m. she suddenly began to feel very rapidly and died within an hour.

A necropsy was performed by Dr. Farnold K. Lane of the Department of Pathology, University of Chicago. The

pathological findings included thrombosis of the mesenteric, celiac, splenic, hepatic, and left gastric arteries and their branches. This apparently resulted from embolism from a mural thrombus on an atheromatous plaque in the descending thoracic aorta.

CASE 3 M K (P H. No 156459), aged 40 years, a white American male, was admitted to the service of Dr D B Phemister in the Presbyterian Hospital on May 30, 1922. The patient first complained of diffuse abdominal distress on the night of May 26, 1922, the pain continued throughout the next 3 days, and on May 30 it became more severe. Examination revealed an acutely ill man who had diffuse tenderness throughout the abdomen with somewhat greater tenderness on the right side. The leucocyte count was 17,500.

Operation was performed at 7:30 p.m. on May 30, by Dr Phemister. The abdomen was opened through a lower right rectus incision. There was a gush of about 3 liters of straw colored clear fluid as the peritoneum was opened. The intestine was everywhere of a bluish tint. The mesentery had dark reddish blue areas in it chiefly at its connection with the small bowel. The involvement extended almost to the ileocecal valve. The vessels of the mesentery were thrombosed. Thirteen feet (396 cm) of the small intestine were resected, and a lateral anastomosis with two rows of silk was done. The peritoneum and skin were closed in the usual manner.

The patient's general condition was fairly good after operation. Early the next morning his general condition became rapidly worse, and death occurred 19 hours after operation.

A necropsy was performed by Dr H. A. Oberhelman who found extensive thrombosis of the superior mesenteric vein and its tributaries, mural thrombus of the aorta at the mouth of the superior mesenteric artery, and generalized serofibrinous hemorrhagic peritonitis.

A careful review of the literature was made of all the conditions that might cause gangrene or infarction of the small intestine and the present series was assembled. After collection of a number of cases of extensive resection, it was soon apparent that the mortality rate and the percentage of good results varied greatly with the different diagnoses. Thus, the results of extensive resection could not be given in a single statement any more than one could give the results of a similar number of laparotomies which included cholecystectomies, gastric resections, hysterectomies, and simple appendectomies. Then, too, certain intra-abdominal disorders required more extensive removal of small intestine than others so that again the results would not be comparable. For convenience in analyzing the results in this series, the following arbitrary classification of cases was made. The case was classified as a death if the patient died within 2 weeks of the operation, a poor result was obtained if death occurred within the first year after operation, and a fair result was considered if the patient had digestive or diarrheal disturbances after operation, or if death occurred later than 1 year as a consequence of the operation. Good results were considered as such only if the author stated there was a good result

with no digestive or gastro-intestinal disturbances, or if the patient was able to return to work as before the resection. In referring to Table I, it can be seen that the greatest number of cases of resection over 200 centimeters occurred in 78 patients with volvulus of the small intestine or *Knotenbildung* of the sigmoid flexure and the small intestine. Incarcerated or strangulated hernia (45 cases), mesenteric thrombosis (34 cases), diseases of the female pelvic organs including uterine perforations with a curette (21 cases), and affections of the mesentery (19 cases) followed in order.

#### VOLVULUS AND KNOTENBILDUNG

The most common cause for extensive resection was volvulus. In this particular condition two entirely different situations must be recognized. Volvulus of the small intestine was the cause for resection in 27 cases (6, 15, 16, 38, 47, 54, 69, 73, 88—7 cases, 92, 93, 138, 140, 144, 157, 161—2 cases, 182, 187, 188, and 194), and although the average length was great (318 cm) this class had a high percentage of good results (55.5 per cent). The second type of volvulus or *Knotenbildung* was described by Falun in 1906 in which a knot formation involved the ileum and the sigmoid flexure. Forty-nine cases (41—11 cases, 47, 48, 88—32 cases, 113, 134, 162, and 187) were collected from the literature in which *Knotenbildung* of the sigmoid flexure and the small intestine required the removal of 200 centimeters or more of small bowel. Kallio has recently written a monograph on this subject, and he was able to assemble 161 examples of intestinal knot formation. Practically all of these cases have been reported in patients living in the region of the Baltic Sea. The highest mortality rate (65.3 per cent) for any particular cause necessitating massive resection of the small intestine occurred with *Knotenbildung* involving the sigmoid flexure and the ileum.

#### STRANGULATED HERNIA

The second most common cause for extensive resection was incarcerated or strangulated hernia. There were 26 examples (4, 7, 9, 11, 15, 49, 61—2 cases, 63, 65, 68, 79, 102, 103, 125, 133, 135, 143, 149, 158, 176, 185, 186, 191 and 192) of inguinal hernia, 6 (31, 36, 40, 62, 151, and 158) of femoral hernia, 6 (33, 57, 61, 76, 129, and 211) of umbilical, and 7 (15, 52, 80, 100, 104, 112, and 152) in which other types occurred or in which the type was not stated. The peculiar type of hernia *en W* occurred five times (79, 102, 103, 151, and 176) in this series, and the mortality was quite high (40 per cent). Pólya, in 1911, collected a group of 62 cases of hernia *en W* or retrograde incarceration in

TABLE I—CONDITIONS REQUIRING MASSIVE RESECTION OF SMALL INTESTINE

Diagnosis	C	D	MC	R	GR	FR	PR	cm	lt	♀	♂
Ulcer and Enterostomy	76	40	13 8	26	20 5	6		268	64	20	
Segment and above	46	33	65	77	20 5	4		200	46		
Small intestine	27	8	20 8	16	20 5			123	26	3	
Perforated hernia	43	11	42	20	21 5	20 6	77	264	11	11	17
Inguinal	46	7	26 5	18	26	5	11 5	265	17	1	17
Femoral	6		20	3		11 5	11	267		1	
Diaphragmatic	4	5	20	3	26 7		26 7	266		1	
Other types or type not known	7			6	26	26 6	14	269			17
Mesenteric thrombosis	34	14	65	20	26	5		200	30	17	
Female pelvic disease	21		20	27	26	5	17	271		11	
Dissecting perforation			26	5	23 5	5	17	213		17	
Other pelvic disease	20		20	2	26	20	20	267		20	
Mesenteric tumor	20		11	14	26 2	20	5	217		5	17
Primary mesenteric tumor	14	3	20	17	26	26 5		214			
Mesenteric adenoma			11 5		11 5			210			
Other conditions							20	217			
Abdominal injuries	26		26 7	20	23 7		5	243	77		
At wounds	6		26					264	5		17
Other conditions	11		26	5	26 7			11	10		
Tuberculosis of the intestine	26		11 5	14	27		11	265		2	
Adhesions or bands			14	6	77			11	6		
Malnutrition	5		77		77		5	773			
Cases not stated	20		20	1	20	11	20	264			5
Total	277	24	11 5	106	26	6	6	205	126	77	26

C—cases, D—deaths, MC—mesenteric perforation, R—resection, GR—percentage of good results, FR—percentage of fair results, PR—percentage of poor results, cm—average length of resection in centimeters, lt—left, ♀—female, ♂—male, 17—cases not stated, 17—rate of 100 patients, 17—rate of 100 patients, 17—rate of 100 patients.

which there was a mortality of 41.9 per cent. thus, the results in the smaller series with resection compares favorably with the results of the disease entity.

#### MESENTERIC THROMBOSIS

Mesenteric thrombosis, as can be expected, contributed a fair number of cases (1, 2, 8, 18—5 cases, 21, 25, 58, 70, 72, 84, 86, 87, 94, 107, 110, 114, 115, 119, 120, 121, 122, 126, 146, 154, 167, 171, 179, 180, 205, 212 and author's cases Nos. 2 and 3) to the total. Elliott performed the first successful enterectomy for infarction due to mesenteric thrombosis when he resected 130 centimeters of small intestine in 1895. Jackson, Porter and Quinby in 1904 collected and reviewed 214 cases of mesenteric embolism and thrombosis. In their series there was only 1 (Greenough's case) massive resection of the small intestine. Forty-seven operations were performed with a mortality of 92 per cent. Trotter brought the

total to 360 cases in 1913. Ackman estimated (1931) there were about 500 cases in the literature. Farah in 1929 collected 86 cases of enterectomy for mesenteric thrombosis with 47 recoveries, however only a small percentage of these were extensive.

#### DISEASE OF THE FEMALE PELVIC ORGANS

Twenty cases of massive enterectomy (30, 32, 33, 50, 53, 56, 59—cases, 77, 108, 116, 127, 143, 155, 163, 168, 71, 207, 208, and 213) were necessary because of disease of the female pelvic organs. The most common cause in this group, of which there were 11 (50, 59—2 cases, 116, 117, 155, 163, 168, 171, 207 and 208) was perforation of the uterus with a curette. This usually occurred at the time of a criminal abortion. There was generally extensive injury to the mesentery associated with prolapse of great lengths of intestine. This class of cases required the removal

of the greatest length of small intestine, and the average length excised was far greater than for any other cause (513 cm). In 3 cases, the almost unbelievable lengths of 820, 750, and 700 centimeters were excised and in each instance the patient recovered.

#### DISEASES OF THE MESENTERY

Derangements of the mesentery contributed 19 cases (12, 17, 35, 90, 91, 92, 98—2 cases, 105, 126, 130, 139, 150, 153, 169, 174, 190, 206, and 210) to the total. Tumors of the mesentery, either primary or secondary, comprised the greater percentage. This class of cases required a rather long excision of small intestine on an average (331 cm), and the percentage of good results was not high (26.3 per cent). It is interesting to note there were 3 cases (35, 92, and 210) in which the small intestine became incarcerated in a slit in the mesentery.

#### ABDOMINAL INJURIES

Abdominal injuries accounted for a number of cases (13, 19, 64, 67, 82, 147, 165, 177, 193, 196, 199, 203—4 cases, and author's case No. 1). It must be agreed that the mortality rate of 18.7 per cent is ridiculously low. In comparison with the mortality in this series, the United States War Department reported 1,928 admissions for injuries to the abdomen and pelvis during the World War with 1,199 deaths or a mortality of 62.2 per cent. War wounds necessitated 5 massive resections, and these (13 and 203) are all reported from the British Army Medical Corps. In the official report of the War Department, the United States had 153,537 admissions for battle injuries during the World War, and only 2 cases (excluding fatal cases) are recorded as "partial loss of the intestine."

#### TUBERCULOSIS OF THE SMALL INTESTINE

Tuberculosis contributed 16 cases to the total (6, 28, 29, 81, 97, 123, 128, 141, 175—7 cases, and 195). There were only 2 deaths, and the reported results were surprisingly good despite frequent statements in the literature that good results cannot be expected in tuberculous patients. Again it may be possible that poor results have not been reported.

#### MISCELLANEOUS CAUSES

Adhesions and bands accounted for 7 cases (10, 77, 89, 131, 157, 159, and 178), and there was a high percentage of good results (71.4 per cent). Miscellaneous causes constituted a total of 12 cases, and this included a variety of conditions: invagination of a polyp (36 and 170), intussusception of the small intestine (15 and 39), ab-

TABLE II—CORRELATION OF AGE AND THE RESULTS IN MASSIVE RESECTION

Age	C	D	M%	R	GR	FR	PR	?
1-10	3	0	00.0	3	100.0			
11-20	15	2	13.3	13	60.0	6.6	13.2	
21-30	57	14	24.5	43	38.6	10.5	8.7	
31-40	44	16	36.3	28	38.6	11.3	2.2	
41-50	38	17	45.8	21	31.6	10.5	10.5	
51-60	27	12	44.4	15	37.0	3.7	7.4	
61-70	22	7	31.8	14	31.8	9.0	4.5	1
71-up	9	6	66.7	3	11.1	11.1		
Not stated	43	13	30.2	6	18.6	2.3	2.3	5
Total	257	86	33.5	165	36.7	8.2	7.8	6

C—cases D—deaths. M%—mortality percentage R—recoveries GR—percentage of good results. FR—percentage of fair results PR—percentage of poor results. ?—fate unknown.

dominal dehiscence (23), colloid carcinoma of the transverse colon with intestinal adhesions (55), gangrene of the ileum (59), intestinal obstruction (96), ileocecal tumor (111), gangrenous appendicitis and gangrenous ileum (142), knot of a free Meckel's diverticulum (157), ileus (160), and appendiceal abscess (201). The remainder (5, 15, 34, 70, 74, 75, 83, 95, 109, and 121) included 10 cases in which the cause for the resection was not stated.

#### AGE

The age was found to vary widely in the 214 instances in which it was mentioned (Table II). The extremes ranged from 8 to 76. Rugg's resection of 330 centimeters in a boy of 8 and Blayney's report of a resection of 253 centimeters in a boy of 10 are cases of the two youngest patients on record. At the other extreme there were 9 patients over 70 years of age. Pólya and Heller each reported a case in patients of 76 years. In passing, it may be noted that Flint successfully resected 100 centimeters of ileum from a male infant of 11 months for gangrene due to an intussusception. Jackson's case of successful resection of 142 centimeters of gangrenous small intestine for herniation through a mesenteric defect has already been mentioned. In consulting the table, it is seen that the greatest number of resections occurred between the ages of 21 and 30, and the next in order was 31 to 40. There was considerable increase in the mortality of the operation above the age of 30 as compared to the results between the ages of 11 and 30. Flint found experimentally that young animals did not withstand resection as well as older dogs. In this clinical series, better results have been recorded under the age of 20, and there

TABLE III—CORRELATION OF THE SEX AND THE RESULTS IN MASSIVE RESECTION

Sex	C	%	D	M%	R	GR	FR	PR	F
Male	26	42.8	56	43.8	86	23.6	1	0	
Female	75	66.8	54	3.8	62	6.4	7	13.8	
Not stated	26	30.4	2	1.9	15	39.4	7	3.7	
Total	77	40.0	86	23.8	163	36.7	8	7.1	4

C—cases; %—percentage of total series; D—deaths; M%—mortality percentage; R—resections; GR—percentage of good results; FR—percentage of fair results; PR—percentage of poor results; F—fatal cases.

is comparatively little difference in the good results obtained between the ages of 21 and 70.

## SEX

The sex was stated in 331 of the 357 cases, and in analyzing the sex incidence nothing of importance was revealed (Table III). There were 156 males and 75 females. The higher mortality in males (43.8 per cent) as compared to that of females (3.8 per cent) can be explained by the higher mortality of mesenteric thrombosis, and volvulus between the ileum and sigmoid flexure in which males predominate. The percentage of good results in the series was relatively the same but the percentage of poor results in females was much more frequent.

## LENGTH OF RESECTIONS

A correlation was made between the amount of intestine removed and the results (Table IV). As can be expected, the greatest number of cases (143) measured between 200 and 300 centimeters, the number diminishing as the length increased. The mortality rate was comparable in any length from 200 to 400 centimeters. In general, it must be admitted that as the amount of intestine removed became longer the results became poorer.

## OPERATIVE PROCEDURES

A correlation was also made between the type of anastomosis and the results (Table V). The best results, as far as operative mortality was concerned, followed lateral anastomosis of the small intestine (20.6 per cent) and lateral anastomosis of the small intestine with the ascending colon (18.7 per cent) whereas lateral anastomosis with a Murphy button showed the poorest figures (60.0 per cent). Cases in which an anastomosis was made had a high mortality rate (64.7 per cent) but it must be remembered that many of these cases were in desperate circumstances at operation, and this procedure was used in an endeavor to conserve time.

TABLE IV—CORRELATION OF THE AMOUNT RESECTED AND THE RESULTS IN MASSIVE RESECTION

Length resected	C	D	M%	R	GR	FR	PR	F
200-299	143	23	23	86	36.8	6.3		
300-399	76	27	35.5	49	31			
400-499	21	17.8	84	37				
500-599		4		12	75	1.7		
600-699		none						
700-799							none	
800-899						none		
Total	237	86	33.8	164	36.7	8	7.1	4

C—cases; D—deaths; M%—mortality percentage; R—resections; GR—percentage of good results; FR—percentage of fair results; PR—percentage of poor results; F—fatal cases.

## METABOLIC STUDIES

Of the series of collected cases, 35 had some sort of quantitative metabolic determinations of the nitrogen, carbohydrate, or fat of the stool (3, 6, 25, 36, 39, 60, 123, 131, 133, 40, 141, 156, 159, 165, 171, 172, 175—7 cases, 178, 183, 185, 86, 187, 190, 195, 201, 205, 12, 213 and author's case No. 1). In all cases in which over 300 centimeters of small intestine were resected there was a definitely abnormal loss of nitrogen in the stool. Excessive fat in the stool was seen in some cases in which as little as 225 centimeters (Allvale's case) were excised. Very few determinations have been made of both the urinary and fecal nitrogen in an attempt to study the nitrogen balance of the patient.

Studies were made of the blood and nitrogen balance in the author's first case by Dr. L. R. Dragstedt. This is the only case in the entire collected series in which any chloride studies were made and in this instance it is enlightening to know the patient was able to maintain his chloride balance adequately despite only 55 centimeters of small intestine interposed between the stomach and the middle of the transverse colon. In addition to the routine laboratory work, the following determinations were made: Blood by drop-son concentration, 7.44; carbon dioxide combining power, 66.45; oximes per cent, blood chlorides (expressed as Cl) 307.4; total base, 148.8; and non-protein nitrogen, 26.7 milligrams per cent. On December 30, the plasma protein was 4.094 grams per 100 cubic centimeters of plasma and by February, 1931 this had fallen to 3.48 grams. Nitrogen balance studies were made in three determinations of 3 days each for 9 consecutive days. The protein lost by stool was

TABLE V—CORRELATION OF THE TYPE OF ANASTOMOSIS AND THE RESULTS IN MASSIVE RESECTION

Type of anastomosis	C	D	M%	R	GR	FR	PR	?
Lateral anastomosis	28	22	28.2	54	44.8	8.9	5.1	
Small intestine (suture)	34	7	20.6	25	55.8	8.8	2.9	2
Small intestine (button)	5	3	60.0	2	20.0		20.0	
Small intestine with ascending colon (suture)	16	3	18.7	13	62.5	12.5		
Small intestine with ascending colon (button)	3	1	33.3	2	66.7			
Small intestine with transverse colon	17	8	47.0	9	17.6	11.8	11.8	
Small intestine with colon	3	0		3	66.7	33.3		
End to-end anastomosis	71	26	36.6	46	47.2	4.1	2.7	
End to end (suture)	53	19	36.5	33	45.3	3.7	1.8	
End to end (button)	19	7	36.8	12	52.6	5.2	5.2	
End-to-side anastomosis	12	3	25.0	0	33.3	33.3		
Small intestine with ascending colon	5	2	40.0	3	20.0	40.0		
Small intestine with transverse colon	2	1	50.0	1	50.0			
Small intestine with colon	1	0		1	100.0			
Undesignated components	4	0		4	25.0	50.0		
Mixer tube in upper portion	1	1	100.0	0				
Anus præternaturalis	17	11	64.7	5	23.5		5.5	1
Type not stated	77	23	29.4	51	15.4	7.7	15.4	3
Total	257	86	33.5	165	36.7	8.2	7.8	

C—cases. D—deaths. M%—mortality percentage. R—recoveries. GR—percentage of good results. FR—percentage of fair results. PR—percentage of poor results. ?—late unknown

found to be 33.9 per cent, 36.0 per cent, and 41.6 per cent in each period (Table VI). These figures might be criticized in view of the work of Mattill and Hawk who showed that bacterial nitrogen constitutes 53.9 per cent of the total fecal nitrogen in normal subjects, but on the other hand it is logical to assume that the bacterial nitrogen would be markedly reduced in a patient with severe diarrhea in which the head of a barium column reached the rectum approximately 4 hours after ingestion.

#### PERIOD OF SURVIVAL

A survey of the cases in the series was made with reference to the period of survival after operation, and the table (Table VII) gives a résumé of end-results in the reported cases. Kallio made a conscientious effort to follow the cases in his article, and a great number of the long survivals are reported in his collection. Two cases have survived 18 years after operation, these are Kallio's case in which patient was operated on by Ignatius who removed 300 centimeters of small intestine and 50 centimeters of ascending colon were resected, and Elfving's case in which patient was operated on by Runeberg who removed 325 centimeters of small intestine. In Zusch

case, Barth operated and resected 316 centimeters of small intestine. This patient was reported alive 14 years after operation. Matthaei's case, in which 530 centimeters of small intestine were excised, died of bronchopneumonia after being in good health for 11 years after operation. The only other reported case with a 10 year survival was the case operated on by Rupp and reported by Frangenheim in which 400 centimeters of small intestine had been removed.

#### DIARRHEA

Diarrhea is the most common and the most disturbing postoperative complication, both clinically and experimentally, and this symptom may be so severe as to cause the death of the patient. Diarrhea caused by extensive resection cannot be controlled by drugs, and the only hope lies in dietary management. Experience and laboratory experiments have borne out the fact that patients can be expected to fare much better on a fat poor, protein adequate, and carbohydrate rich diet.

#### EXPERIMENTAL STUDIES

Senn was perhaps the first individual to do experimental work on resection of the small intestine.

TABLE VI.—NITROGEN BALANCE STUDIES IN CASE 1

Date	Weight	Food Ingested			Calories	Urea N Oxides	Fecal N Gases	Urine Excretion	Residue Loss, %
		C	P	F					
1-9-31	22 6 Kg	642	30	23	1236	4			
1-10-31	22	774	31	23	1296	6.54			
1-11-31	22	666	43	46	1266	26	7.77	26.26	22
1-12-31	22 6	764	46	27	1427	4.64			
1-13-31	22 7	666	29	26	664	6			
1-14-31	22 3	647	44	47	967	3.66	7.23	27.66	26
1-15-31	22 5	76	43	43	1267	6.66			
1-16-31	22 6	666	66	24	1774	26			
1-17-31	22	664	22	27	1662	3.62	3.64	26	41.6

time. In 1883, he performed enterectomies on 4 dogs and 3 cats and, from these 7 experiments, he concluded that excision of more than one-third of the length of the small intestine was dangerous to life. Monari, after a series of resections on dogs in 1896 believed that seven-eighths of the small intestine could be removed with safety. Erlanger and Hewlett studied the problem in 1901 and they decided that dogs with 70 to 83 per cent of the combined jejunum and ileum removed may live indefinitely after recovery from the operation. In 1907 Evans and Brenner performed resections on dogs, and from their experiments they con-

cluded that dogs would survive 50 per cent removal of the small intestine almost invariably and that they would tolerate 67 per cent removal with the best of care. They stated that there was no hypertrophy of the remaining intestine in the most extensive enterectomies. Flint believed that dogs could withstand a resection of 50 per cent of their small intestine and return to normal, but that the animals did not return to normal even though they survived the operative removal of 75 per cent of the small intestine. He also contended that there was a hypertrophy and hyperplasia of the remaining small intestine, and he termed this change a compensation. Wilkerson reported on a number of experiments in 1915. He found that proteins and fats were not well digested in the first 4 weeks after resection of two-thirds of the small intestine in dogs, but that the animals regained this ability to a certain extent later. He found that dogs died from inanition when 70 to 80 per cent of the small intestine was removed. Kuns and Molitor also came to the conclusion that 70 per cent represented the limits of small intestinal resection in dogs.

## CONCLUSION

In the collection of 257 cases of extensive enterectomy it is obvious that the surgeon is dealing with patients who are desperately ill. It is logical to conclude that the mortality rate of 33.5 per cent does not represent the true operative mortality of this spectacular procedure because of the tendency to report only the successful cases. Good results after survival of the operation depend on the condition and length of the small intestine remaining, on the disease condition necessitating the massive resection, and on the feeding of a diet poor in fat, adequate in protein, and rich in easily assimilable carbohydrates. From a study

TABLE VII.—PERIOD OF SURVIVAL AFTER MASSIVE RESECTION OF THE SMALL INTESTINE

Time	Cases reported	Deaths	Good	Fair	Poor results
to 3 months	13	7 <sup>a</sup>	24		
3 to 6 months					
6 to 12 months	26	7 <sup>b</sup>	24	6	6
year			25		
year 1	11	7	7		
year 2	20		6		
year 3					
year 4					
year 5					
2 years					
3 years					
4 years					
5 years					
6 years					
7 years					
8 years					
9 years					
10 years					
11 years					
12 years					
13 years					

<sup>a</sup> none died of causes not referable to the operation  
<sup>b</sup> none died of causes not referable to the operation

of the total series the postoperative results were reviewed in an attempt to answer the question, "How much of the small intestine can be removed and still allow the patient to live and return to normal health?" The prepared tables do not give a direct answer to this query so that another approach to the problem was made. It was found that a total of 86 cases with subsequent good results had an average resection of 310 centimeters, this constituted an average of 47.2 per cent of the total small intestinal length (657 cm) found in a study of 1,161 cases. In 21 cases classified as fair results, an average resection of 367 centimeters, or 55.8 per cent of the total length of small intestine, had been done. Fifteen cases with poor results had an average resection of 348 centimeters, or 52.9 per cent of the average total small intestinal length. A conservative estimate as to the limits of small intestinal resection from the foregoing analyses would be as follows: Discounting the dangers of the operation itself and its concomitant possible complications, a patient can withstand a massive resection of 33 per cent of the length of the small intestine and expect the digestive tract to return to normal function, 50 per cent removal constitutes the upper limit of safety in extensive enterectomy, and resections above 50 per cent must necessarily obtain poorer results even though an exceptional case may be better than predicted.

## SUMMARY

1. Three cases of massive resection of the small intestine are reported.
2. A total of 257 cases of massive resection of the small intestine was collected from a review of the literature, and an analysis of the collected series was made.

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## BIBLIOGRAPHY

1. ACKMAN, F. D. Occlusion of the mesenteric arteries with the report of five cases. *Canadian M. Ass. J.*, 1931, 25: 657-663.
2. ADDISON, OSWALD L. A case of thrombosis of a considerable portion of the superior mesenteric vessels without any discoverable cause. *Brit. J. Surg.*, 5: 173-174.
3. ALBU, A. Ueber die Grenzen der Zulaessigkeit ausgedehnter Darmresektionen. *Berl. klin. Wchnschr.*, 1901, 38: 1248-1252.
4. ALLEN, E. S. Report of cases of intestinal resection. *Kentucky M. J.*, 1923, 21: 267-274.
5. AMOUR. Quoted by Ghedini from Nigrisoli's series, loc. cit.
6. AXHAUSEN, G. Ueber die obere Grenze fuer die Zulaessigkeit ausgedehnter Duenn darmresektionen. *Mitt. u. d. Grenzgeb. d. Med. u. Chir.*, 1909, 21: 55-66, also *Deutsche med. Wchnschr.*, 1909, p. 145.
7. BACKER, ISTVAN. Ausgedehnte Darmresektion. *Orvosi hetil.*, 1931, 1: 312-313.
8. BANER, KAI. Ein Fall von Mesenterialgefassverstopfung mit Resektion von 435 cm. Duenn darm. *Hosp.-Tid.*, 1932, pp. 415-452. Abstracted in *Zentralorgan f. d. ges. Chir.*, 1932, 58: 709.
9. BARACZ, ROMAN VON. Bruch einklemmung complicirt durch Thrombose der Vena mesenterica superior. *Arch. f. klin. Chir.*, 1907, 83: 478.
10. BASTIANELLI. Quoted by Ghedini from Nigrisoli's series, loc. cit.
11. BEDARIDA, NYNO V. Occlusioni intestinali a duplice sede. *Arch. ital. di Chir.*, 1928, 22: 634-644.
12. BELL, GEORGE, and INGLIS, K. A case of sarcoma of mesentery, successful removal involving resection of ascending colon and 237.5 cm. of ileum with pathological report. *M. J. Australia*, 1923, 1: 375.
13. BELL, GORDON. Resection of the small intestine for war wounds. *J. Roy. Army Med. Corps*, 1921, 36: 351-360.
14. BENKEE. Ueber die Laenge des Darmkanals bei Kindern, sowie ueber die Capacitaet des Magens Neugeborener. *Deutsche med. Wchnschr.*, 1880, pp. 448-449.
15. BERGMAN. Quoted by Ghedini from Nigrisoli's series, loc. cit.
16. BERKOFER, K. Erfahrungen bei der operativen Behandlung des abgeklemmten brandigen Darmes. *Deutsche Ztschr. f. Chir.*, 1911, 109: 133-159.
17. BERNAYS, AUGUSTUS C. Sarcoma of the mesentery; resection of 119 inches of small intestine, recovery. *Ann. Surg.*, 1902, 35: 790-801, 835.
18. BLACKBURN, J. H. Mesenteric thrombosis and embolism, report of 36 cases. *South. M. J.*, 1916, 9: 810-819.
19. BLAYNEY, ALEXANDER. On the removal of great lengths of intestine. *Brit. M. J.*, 1901, 2: 1456-1458.
20. BOECKEL, JULES. Resection de deux metres d'intestin (ileon, caecum, et colon ascendant) dans une forme d'appendicite non encore decrite. *Bull. Acad. de med., Par.*, 1912, 68: 241-245.
21. BONNOT, EDMOND. Mesenteric thrombosis with 88 inches of intestine resected. *Med. Rec.*, 1918, 93: 502.
22. BORNSTEIN, FRITZ. Ueber morphologische Veraenderungen nach ausgedehnter Duenn darmresektion. *Arch. f. path. Anat.*, 1933, 291: 921-936. See also Matthaei, loc. cit.
23. BRENNER, A. G. Extensive resections of small intestines. *Ann. Surg.*, 1929, 89: 675-681.
24. BROHIE. Extensive resection of small intestine, anastomosis of stomach and lower ileum. *Bruxelles med.*, 1920, 9: 685-687. Abstracted by W. F. Prior & Co., Inc.
25. BROUGRAM, E. J. A case of resection of 11 1/2 feet of small intestine. *Surg., Gynec. & Obst.*, 1907, 4: 782.
26. BRUETT. Embolie und Thrombose der arteria mesenterica superior. *Zentralbl. f. Chir.*, 1922, 49: 611. See Schumm and Papendieck, loc. cit.
27. BRYANT, J. Observations upon the growth and length of the human intestine. *Am. J. M. Sc.*, 1924, 167: 499-520.
28. CAIRD. Quoted by Ghedini from Nigrisoli's series, loc. cit.
29. CANADAY, JOHN E. Long resections of the intestine. *Ann. Surg.*, 1919, 69: 423-431.



- 30 CANTOLARI, ENRICO. Resezione di due nodi, trenta centimetri di intestino tenue ed intersezione addominale per lesioni traumatiche di origine ostetrica. *Giornale Chir. d'op.* 9, 40, 385-388.
- 31 CHILDS, CHARLES P. A case of successful resection of ileo and one half feet of small intestine for proptosis. *Brit. M. J.* 1907, 21, 891-892.
- 32 CHOWANET, H. S. Case of hernia through rupture of the uterus necessitating resection of 3 feet of intestine. *Ann. J. Gynec. & Obst.* 1904, 43-51.
- 33 CURET. Quoted by Ghedou from Nagelsch' series, loc. cit.
- 34 DEKORNEY. Reference by Istomlin. *Russ. med. Rundschau* 9, 9, 339. Cited by Soyuzmen, loc. cit.
- 35 DELERKAMP. Ueber ausgebreitete Duodenalnekrosen. *Beitr. z. klin. Chir.* 1910, 5, 70-160.
- 36 DIERK, WOLFGANG. Ausgedehnte Duodenalnekrose mit Ausgang in Hohlraum. *Wien. klin. Wochenschr.* 1907, 50, 1549-1551.
- 37 IDER. Ueber die Prognose ausgebreiteter Duodenalnekrosen. *Mitt. d. Grenzgeb. d. Med. u. Chir.* 19, 4, 146-153.
- 38 DOKSCHER, HENRIKUS. Kann der Mensch ohne Duodenum leben? *Kasustische. Beitrag. Zentralbl. f. Chir.* 1903, 30, 300-304.
- 39 DOWSE, A. R. E. Ausgedehnte Duodenalnekrose mit Amputation der Nahrungsgänge. *Dissertation, Hamburg*, 91.
- 40 DREKSMANN. Ueber grossere Duodenalnekrosen. *Beitr. klin. Wochenschr.* 1909, 30, 157-159.
- 41 EASTMAN, A. R. Kasustische Beitrag zur Kenntnis von Knechtbildung zwischen transversem und flexurem duodenale. *Funka. Lab. stit. handl.* 1914, 66, 603-606. Abstracted in *Internat. Abstr. Surg.* 1915, 4.
- 42 IDER. Kasustische Beitrage zur Kenntnis der Knechtbildung zwischen Duodenum und Flexura sigmoidea. *Acta chir. scand.* 1915, 59, 185-187.
- 43 ELLIOTT. Operative relief of gangrene of the intestine due to occlusion of the mesenteric vessels. *Ann. Surg.* 1895, 21, 9-23.
- 44 ELLIOTT. Reference by Istomlin. *Russ. med. Rundschau* 9, 9, 339. Cited by Soyuzmen, loc. cit.
- 45 ERLINGER, JOSEPH, and HENRIETT ALBERT W. A study of the metabolism in dogs with shortened small intestines. *Ann. J. Physiol.* 1904, 6, 1-30.
- 46 E. vs. HENRIETT M. and BERNARD, A. G. Resection of the small intestine in the dog. *Johns Hopkins Hosp. Bull.* 1907, 8, 477-480.
- 47 FALTUS, R. Kasustische Beitrage zur Kenntnis der Knechtbildung des Duodeni. *Deutsche Zeitschr. f. Chir.* 1906, 84, 477-487.
- 48 IDER. Beitrag zur Kenntnis von Knechtbildung. *Funka. Lab. stit. handl.* 1909, 51, 530-536.
- 49 FANTINO. Contributo allo studio delle cause meccaniche intestinali. *Gazz. med. di Torino* 1896, 47, 8. Abstracted in *Centralbl. f. Chir.* 1904, 3, 514.
- 50 IDER. Nuovo contributo allo studio delle cause meccaniche intestinali. *Riforma med.* 1905, 4, 66-64. Abstracted in *Giornale f. Chir.* 1905, 8, 715.
- 51 FABIAN, JEAN. L'infarction hémorragique de l'intestin. *Yb. de med. Paris*, 1900.
- 52 FERNER, A. Gabelstiel Fall von ausgebreiteter Darmnekrose. *Centralbl. f. d. Grenzgeb. d. Med. Chir.* 1906, 9, 70. Quoted from Hachtenschwager, loc. cit.
- 53 FLATER and SCHWENGER. Ueber die Prognose von gedehnten Duodenalnekrosen. *Beitr. klin. Wochenschr.* 1909, 30, 740-751.
- 54 FLEISCHMANN, CARL. Ueber ausgebreitete Duodenalnekrosen. *Mitt. d. Grenzgeb. d. Med. Chir.* 1917, 10, 451-468.
- 55 FLEET, J. M. The effect of extensive resections of small intestine. *Johns Hopkins Hosp. Bull.* 19, 2, 87-144.
- 56 FLORENTIN P. Bericht ueber einen Fall grosser Duodenalnekrose. *Zentralbl. f. Chir.* 1915, 43, 597-598.
- 57 FOM, H. L. Intestinal resection in cases of acute intestinal hernia. *Surg. Gynec. & Obst.* 1915, 30, 263-270.
- 58 FOWLER, O. S. Duodenal of superior mesenteric thrombosis. *Southwestern Med.* 1916, 144-155. See Wilbert, loc. cit.
- 59 FRANKFURT. Spetiology nach ausgebreiteter Duodenalnekrose. *Arch. f. klin. Chir.* 1915, 38, 146-150.
- 60 FRANKLIN CLAUDE. Strangulated hernia. *Review of 148 cases. Brit. J. Surg.* 1917, 5, 76-101.
- 61 FRAU. Histologische Beobachtungen zur benedert Betrachtung der Radikaloperationen. *Deutsche Zeitschr. f. Chir.* 1909, 51, 1-10.
- 62 FRIEDMAN, P. L. Ueber den Nature der funktionellen Ausdehnung grosser Duodenalnekrosen bei septischen Peritonitis. *Med. Klin.* 1905, 13-16. See also Dierk, loc. cit. (37).
- 63 FRIEDL, J. Verfall und Darm chirurgie aus der Privatklinik. *Berlin* in den 4 Jahren. 1894-1901. *Mischel. Rev. Abstracted in Jahrbuch f. Chir.* 1904, 4, 634.
- 64 GARDNER, E. L. and BURNETT, O. W. Extensive resection of small bowel following trauma in which 26 cm. were removed with recovery. *Canadian M. Ass. J.* 1911, 5, 300-303.
- 65 GEDOU, ANTOINE. Extensive resection of intestinal wall. *Intestine. Chir. Chir.* 1905, 3, 7-24. Abstracted by W. F. Price & Co. Inc.
- 66 GROSS, CHARLES LAWSON. A study of 600 operations for acute intestinal obstruction and gangrenous hernia. *Ann. Surg.* 1900, 3, 456-514, 670-707.
- 67 GROSS, F. P. and TURN, G. de. Resektion intestinalis exsupta per grave transmigration abdominali. *Berlin med.* 1911, 38, 77-85.
- 68 GROSS, JOSEPH. Ueber Verfall der Mesenterialgefasse nach Mitteilung einer operativ gebildeten Falte. *Wien. klin. Wochenschr.* 9, 4, 351-352.
- 69 GROSS, RUDOLF. Erfolgreiche Resektion von 1 m. Dünndarm wegen Verfall und seiner Entzündung. *Deutsche Zeitschr. f. Chir.* 1905, 77, 605-6.
- 70 GROSS, T. ELON, G. Discussion on the diagnosis and treatment of injuries of the intestine. *Brit. M. J.* 1901, 2, 630-643.
- 71 GROSS, JOSEPH, & B. See Jackson et al., loc. cit.
- 72 GROSS, LOUIS A. Thrombosis of the superior mesenteric artery. *Ann. Surg.* 1905, 4, 303-303.
- 73 GUTAL, J. Quatre cas de volvulus du grêle. *Bull. et Mém. Soc. med. de Chir.* 1900, 55, 147-154. Abstracted in *Internat. Abstr. Surg.* 1901, 5, 30-3.
- 74 HAGARD, H. D. Personal communication to Carlsbad.
- 75 HART. Quoted by Ghedou from Nagelsch' series, loc. cit.

- 76 HAHN, EUGEN Ueber einige Erfahrungen auf dem Gebiete der Magendarm chirurgie Deutsche med Wchnschr, 1897, 23 650-653
- 77 HARRIS, GEORGE R Resection of nearly 8 feet of gangrenous intestine, recovery Med Rec, 1902, 62 563-566
- 78 HAYES Quoted by Harris, loc cit.
- 79 HELLER, E Zur Kenntnis der retrograden Darminkarzeration Med Klin, 1908, 4 151-155
- 80 HOFMANN, M Ueber ausgedehnte Darmresektionen. Arch f klin Chr, 1924, 131 251-268
- 81 HOFMEISTER. Quoted by Ghedini from Nigrisoli's series, loc. cit.
- 82 ISELIN Peritonisierung des Mesenterialstumpfes mit freiem Netz bei ausgedehnter Darmresektion Zentralbl f Chr, 1912, 39 739-740
- 83 ISTOMIN Russ med Rundschau, 1910, 8 329 Quoted from Sovesuma, loc cit
- 84 JACKSON, J M, PORTER, C A and QUINBY, W C Mesenteric embolism and thrombosis J Am M Ass, 42 1469-1475, 43 25-29, 110-114 183-187
- 85 JACKSON, R H Extensive resection of small intestine in an infant. Surg, Gynec & Obst, 1925, 40 55-61
- 86 JERAULD, E N C, and WASHBURN, W W Extensive resection of small intestine, removal of 19 feet of ileum and jejunum J Am M Ass., 1920, 92 1827-1830
- 87 JUDIN S Ein operativ geheilter Fall akuter Thrombose der Mesenterialgefäße Novy chirurg Arch, 1926, 11 140-145 Abstracted in Zentralbl f d ges Chr, 1927, 39 295-296
- 88 KALLIO, K E Die Knotenbildungen des Darmes Acta chirurg scand, 1932 70 Suppl 21 1-278
- 89 KARLOV, A Bulbrack efter appendicetopertion Hygiea, 1903 63 460-471
- 90 KARSTROEM, W Fibromyoma retroperitoneale Laparotomie Resektion des Duennndarms (20 cm) Exstirpation des Tumors Heilung Hygiea, 1902 p 472 Abstracted in Jahresbr f Chr, 1902 8 657
- 91 KENGLA, LOUIS A Fibroma of mesentery Occidental M Times, 1902, 16 140-141
- 92 KIMBAROVSKIJ, M Zur Frage ausgedehnter Resektionen des Duennndarms Novy chirurg Arch 1931, 22 551-555 Abstracted in Zentralorgan f d ges Chr, 1931-1932 56 815
- 93 KIRKWOOD W L Torsion of the small intestine, resection of 8 feet of intestine, recurrence of torsion Med. J Australia 1915, 2 49-50
- 94 KOCHER. Quoted by Ghedini from Nigrisoli's series, loc cit
- 95 KOCHER, TH Textbook of Operative Surgery 3d Eng edit, pp 625-626 A. & C Black, 1911
- 96 KOEBERLE Résection de deux metres d'intestin grele Guérison Bull de Acad de méd 1881, 8 249-250
- 97 KOPFSTEIN W Beitrag zu ausgedehnten Darmresektionen Wien med Bl 1910 33 16
- 98 KUKULA Ueber ausgedehnte Darmresektionen Arch f klin Chr 1900 60 887-950
- 99 KUNZ, HUBERT and MOLLITOR, HANS Ueber die Ursachens der Ernährungsstörungen nach ausgedehnten Duennndarmresektionen und ihre Behandlung Arch f exper Path u Pharmacol 1928, 132 50-62 Abstracted in Zentralorgan f d ges Chr, 1928, 44 463
- 100 KUSCHEWA, M N, and MALINOWSKY, N N Eine Operation der Hernia duodenojejunalis incarcerata mit ausgedehnter Resektion des Duennndarms Zentralbl f Chr, 1927, 54 525-528, Zentralorgan f d ges Chr 1927, 38 315
- 101 LAMB Quoted by Brvant, loc. cit
- 102 LANGER, ARMIN Ueber retrograde Inkarceration des Darmes Wien klin Wchnschr., 1903, 16 475-478
- 103 LAUENSTEIN, CARL Ist es moeglich "Darmschlingen im eingeklemmten Bruch" zu diagnostizieren? Zu gleich ein neuer Beitrag zu der Pathologie der "Hernie en W" resp der "retrograden Darminkarzeration" Deutsche Ztschr f Chr, 1909, 100 155-180
- 104 LAUWERS Des résections étendues de l'intestin grele J de chir et ann belge de chir, 1901, 1 739-752
- 105 LEXER, E. Operation eines Mesenterialfibromes mit ausgedehnter Resektion des Duennndarms Berl klin Wchnschr, 1900, 37 4-5 See also Albu, loc cit
- 106 LIEBLEIN, VIKTOR. Einige Bemerkungen zur Frage der Prognose der ausgedehnten Duennndarmresektionen Mitt. a d Grenzgeb d Med u Chr, 1911, 23 1-12
- 107 LINDNER, H Ueber Thrombose der Mesenterialgefäße Berl klin Wchnschr, 1905, 42 Fest-Num, 5-7
- 108 LITTLEFIELD, JOHN R. Resection of 13 feet of ileum J Am M Ass, 1919, 73 835-836
- 109 LONG, J W Personal communication to Cannaday
- 110 LOOP R G Mesenteric vascular occlusion with report of 9 cases in which operation was performed J Am M Ass, 1921, 77 369-373
- 111 LORENZ, H Fine der ausgedehntesten Darmresektion die bisher an Lebenden ausgeführt wurden Wien klin Wchnschr, 1906, 19 610-611
- 112 LUKESOVA Incarcerierte gangränöse Hernien im Deutschbroder Krankenhaus, 1898-1920 Casop lek. česk, 60 480-483 Abstracted in Zentralorgan f d ges Chr, 1921, 14 424
- 113 LUNDBERG SVEN Ein Fall an ausgedehnter Duennndarmresektion Acta chirurg Scand, 1920, 52 413-435
- 114 MCGUIRE, EDGAR R. Successful removal of over 21 feet of small intestine Surg, Gynec. & Obst., 1913, 16 40-42
- 115 MCGUIRE, STUART Mesenteric thrombosis with report of two cases. Virginia M Month, 1923, 50 23-26
- 116 MATTHAEI, F Ueber ausgedehnte Duennndarmresektion und ihre Folgen Arch f path Anat, 1925, 254 345-353 See also Fiedler Zentralbl f Gynaek., 1923, 47 180 and Bornstein, loc. cit.
- 117 MATTILL, H. A., and HAWK, P B A method for the quantitative determination of fecal bacteria J Exper Med, 1911, 14 433-444
- 118 MAYDL. Quoted from Kukula's series and by Ghedini, loc. cit
- 119 MEYER, JOSEPH L Mesenteric vascular occlusion Ann Surg, 1931, 94 88-96
- 120 MICHAEL, P R Thrombosis venae mesentericae Nederl Tijdschr v Geneesk., 1925, 69 584-588 Abstracted in Zentralorgan f d ges Chr 1926 36 410
- 121 MITCHELL, A B Discussion Med Rec, 1909, 76 330
- 122 MITCHELL, J F Mesenteric thrombosis Ann Surg, 1923, 77 299-305, Ty South Surg Ass, 1923, 35 223-240
- 123 MRAKE, H Ueber ausgedehnte Darmresektion mit einer kurzen Bemerkung ueber die normale Laenge des Jejunum-Neum bei dem Lebenden Arch. f klin Chr, 1910, 93 768-783



- 173 SEYB, NICHOLAS. An experimental contribution to intestinal surgery with special reference to the treatment of intestinal obstruction. *Ann Surg*, 1888, 7 99-115
- 174 SHEPHERD, FRANCIS J. Successful removal of an enormous mesenteric tumor and nearly 8 feet of intestine. *Brit. M J*, 1897, 2 966-968
- 175 SHIMA, K. Allgemeine Stoffwechseluntersuchungen nach totaler Magenextirpation und ausgedehnter Darmresektion. *Beitr. z. klin. Chir.*, 1931, 153 275-299
- 176 STEBERT. Inaugural Dissertation, Koenigsberg. Cited from E. Polya, loc. cit.
- 177 SIMON, R. Triple déchirure traumatique du mésentère, résection de 2m 10 de jejuno-ileon, guérison. *Gaz. méd. de Strasb.*, 1923, 81 661-662, Personal communication
- 178 SINCLAIR, N. F. Remarks on extensive resection of small intestine with notes on a case. *West Lond. M J*, Lond., 1924, 29 24-29
- 179 SÖVALL, S. Ueber Embolieder Arteria mesenterica superior mit Anschluss eines Erfol operierten Falles. *Acta chirurg. scand.*, 1927, 61 577-586
- 180 SMIDT, HANS. Ausgedehnte Darmresektion bei arteriell-embolischem Darminfarkt. *Deutsche Ztschr. f. Chir.*, 1919, 150 399-408
- 181 SMITH, WILBUR. Superior mesenteric thrombosis. *Southwest. Med.*, 1928, 12 549-555. Fowler, loc. cit.
- 182 SOHN, ADOLF. Ausgedehnte Duenn darmresektionen. *Deutsche Ztschr. f. Chir.*, 1923, 181 403-412. Abstracted in *J. Am. M. Ass.*, 1923, 81 1914
- 183 Idem. Zur Frage der Dauerheilung nach ausgedehnten Duenn darmresektionen. *Deutsche Ztschr. f. Chir.*, 1927, 201 263-265
- 184 SOVESIMA, A. Experimentelle und literarische Studien ueber die ausgedehnten Duenn darmresektionen. *Deutsche Ztschr. f. Chir.*, 1911, 112 424-466
- 185 SPASSOKUKOZKAJA, N. J. Ein Fall von ausgedehnter Duenn darmresektion. *Centralbl. f. Chir.*, 1906, 33 687
- 186 STAHLIN, E. Resection of 10 feet 2 inches of small intestine with recovery. *Ann Surg.*, 1907, 45 49
- 187 STASSOFF, B. Experimentelle Untersuchungen ueber die kompensatorischen Vorgaenge bei Darmresektionen. *Beitr. z. klin. Chir.*, 1914, 89 527-586
- 188 STOLZ. Ausgedehnte Darmresektion wegen Gangraen. *Deutsche med. Wchnschr.*, 1909, 35 744
- 189 Idem. Spaetresultat einer ausgedehnten Duenn darmresektion. *Berl. klin. Wchnschr.*, 1910, 47 1685, *Muenchen med. Wchnschr.*, 1910 57 1716
- 190 STORR. Ueber die Zulaessigkeit ausgedehnter Duenn darmresektionen. *Deutsche Ztschr. f. Chir.*, 1907, 87 313-319
- 191 STUCKEY, LEO. Zur Kenntnis der retrograden Inkarnation. *Deutsche Ztschr. f. Chir.*, 1910, 105 545
- 192 SYKING. Cecum Duenn darm Volvulus in eingeklemmter Hernie. *Beitr. z. klin. Chir.*, 1913, 82 695-701
- 193 TANTZSCHER. Quoted by Ghedini from Nigrisoli's series, loc. cit.
- 194 THON. Ueber Knotenbildung des Duenn darms. *Deutsche med. Wchnschr.*, 1900 35 742
- 195 TOMA, R. Ueber ausgedehnte Resektion des Duenn darms und zugleich ein Beitrag zur Stoffwechseluntersuchung des betreffenden Falles. *Mitt. a. d. med. Fak. d. k. Univ. Kyushu Fukuoka*, 1917, 3 373-390
- 196 TOOMBS, P. W. Resection of intestine following gunshot wound of abdomen. *Railway Surg. J.*, 1914, 21 98-102
- 197 TREVES, FREDERICK. The anatomy of the intestinal canal and peritoneum in man. *Brit. M J*, 1885, 1 415-419
- 198 TROTTER, L. B. C. Embolism and thrombosis of the mesenteric vessels. Cambridge University Press, 1913
- 199 TRZEBICKI, RUDOLF. Ueber die Grenzen der Zulaessigkeit der Duenn darmresektion. *Arch. f. klin. Chir.*, 1894, 48 56-92
- 200 TUOMIKOSKI, VIILJO. Zur Kenntnis der Ausnutzung der Nahrung nach Darmverkurzungen. *Sandin. Arch. f. Physiol.*, 1928, 54 249-320
- 201 TURCK, RAYMOND C. Intestinal resection successful removal of more than 12 feet of bowel with observations on the subsequent metabolism. *New York M J*, 1914, 99 316-319
- 202 VAN VERTS, M. J. Exclusion de la plus grande partie de l'intestin pour un anus contre nature. *Bull. et mém. Soc. nat. de Chir.*, 1903, 29 610-619
- 203 WALLACE, CUTIBERT. A tabular statement of five hundred abdominal gunshot injuries. *J. Roy. Army Med. Corps*, 1916, 26 802-806
- 204 War Department. The Medical Department of the United States Army in the World War. War Department, 1927, vol. 2, Surgery, Part 1
- 205 WATSON, P. Case of extensive resection of small intestine with clinical study of recorded cases. *Edinburgh M J*, 1923, 30 174-184
- 206 WEBER, P. F. Sarcoma of mesentery, its extirpation with 8 1/2 feet of small intestine, peritonitis, death. *Med. Rec.*, 1900, 57 1137-1138
- 207 WERELIUS, A. Successful resection of 12 feet and 2 inches of the ileum in case of criminal abortion. *J. Am. M. Ass.*, 1927, 48 945
- 208 WHITALL, J. DAWSON. Extensive removals of intestine. Report of a case of recovery after resection of 10 feet 8 inches of the ileum. *Ann Surg.*, 1911, 54 669-672
- 209 WILDEGANS, H. Disturbances of metabolism after extensive resections of small intestine. *Deutsche med. Wchnschr.*, 1925, 51 1558-1561. Abstracted in *J. Am. M. Ass.*, 1925 85 1436
- 210 WOHLGEMUTH, KURT. Ueber Tetanus nach Operationen (Gleichzeitig ein Beitrag zur Kasuistik der angeborenen Mesenteriallueken und der ausgedehnten Duenn darmresektionen). *Arch. f. klin. Chir.*, 1923 123 400-414
- 211 WOOD, W. Q. Case of extensive resection of the small intestine. *Edinburgh M J*, 1910 n.s. 25 61-62
- 212 WULSTEN, J. Heilung einer Thrombose der Vena mesenterica superior durch Resektion des gesamten Duenn darms. *Zentralbl. f. Chir.*, 1910, 50 3155-3159
- 213 ZUSCH. Stoffwechsel nach ausgedehnter Duenn darmresektion. *Deutsche med. Wchnschr.*, 1909, 35 739

## EDITORIALS

### SURGERY GYNECOLOGY AND OBSTETRICS

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NOVEMBER, 1935

#### THE TREATMENT OF MALIGNANT TUMORS OF THE UPPER JAW AND ANTRUM FIFTEEN YEARS OF PROGRESS

IN the treatment of malignant tumors, concerted effort by a group of workers treating a large number of patients in a limited field may obtain results that seem almost unbelievable. This point is well illustrated in a monograph by L. George Ohngren, *Malignant Tumors of the Maxillo-Ethmoid Region* in which was reported the work of Gunnar Holmgren's service at the Sabbatsberg Clinic, Stockholm. A complete review of the foreign and American literature has been made and those workers credited who have participated in the development of the method of treatment.

Ohngren traced the development of the treatment of these tumors. At first resection of the jaw was employed; the operative mortality was considerable and few patients remained free of the disease. He then traced the changes that have produced the improved results. The handling of these cases was placed under the direction of those interested in the special field rather than the general surgeons who took care of them previously.

At first pure surgical treatment was employed as a routine method, and the results were poor. Then roentgen rays and radium were used in conjunction with surgical treatment but still the results were not much better. The use of soldering irons or *ferro* candens was then employed and this was followed by the employment of large electrocauteries. Finally in 1925 electro-surgery was used, and in 1927 radium was employed in addition to electro-surgery. In this way much has been accomplished in the care of this group of tumors as compared to the comparatively poor results from surgical treatment alone.

Ohngren in studying tumors of the upper jaw and antrum has used an original classification and included three factors: (1) the more or less favorable position of the tumor; (2) the greater or lesser degree of histological malignancy; and (3) the presence or absence of metastasis. In charting the more or less favorable position of the tumor which of course is a large factor in its curability, he uses a plane which passes from the inner canthus in a direction backward and downward to the angles of the mandible. In this way he has a superior posterior group and an inferior anterior group. It is readily seen that the inferior anterior group of tumors are much more easily accessible to removal and may get to be of large size without invading areas that make their removal impossible than the superior posterior group. Each of these groups Ohngren again divides into a lateral and medial group thus making four groups in all.

The difficulty in gaining access to the medial superior posterior group makes the outlook for them poorest of all, regardless of the type

of malignant tumor In reviewing the results in 149 cases in which operation was performed, Ohngren classifies them as to position in determining the so called cures Histological studies have been made in all cases, and in a very thorough manner he has reviewed the results as related to the particular type of tumor present As would be expected, if recurrence is going to take place, it usually occurs in the first year after operation In this series there were more than four times as many recurrences in the first year as later The fact that it was possible to follow all of these cases makes the report very valuable

The striking improvement in treatment of these tumors over what it was 15 years ago may be appreciated when it is noted that 38.5 per cent of 5 year cures of malignant tumors in this region are reported in this monograph One must remember, too, that in many of the earlier cases patients were treated during the transitional period, when the technique had not been perfected, so similar patients treated today would probably be handled better

Future reports of this work should be still better It is by such work as this that advances are made in our efforts to control malignant diseases

GORDON B NEW

### CONTROLLING GAS PAINS

EVERY intra abdominal operation offers the opportunity of a potential ileus meaning 'obstruction of the bowel attended with severe colicky pain' (Stedman) Short of an actual obstruction, either dynamic or adynamic, the normal peristaltic action of the intestines is usually inhibited the first few hours following operation, but early on the second day intestinal activity is increased, producing what is generally referred to as 'gas pains' These occur in greater or less degree even in the simplest operations within the abdomen They are

never regarded seriously unless they persist and result in over distention with continued pain or, as a further phase, a paralytic ileus with decreasing pains Such conditions present evidence of abnormal complications and are to be dealt with according to indications as outlined in the work of recent investigators

We are not concerned here with the management of intestinal obstruction We are interested in methods of controlling the ordinary "gas pains" associated with the average abdominal operation Since they are due to overactivity of the natural peristalsis of the bowel and since the suppression of the normal intestinal movements would be unwise, it is better to control the pains than to stop them entirely

In the usual case there is no distention, merely the corkscrew cramps running about at intervals over the abdomen, after the general bodily discomfort and the incisional pain have somewhat abated The suffering may be acute even when the abdomen is perfectly flat, free from any accumulation of gas The only justification for the term "gas pains," is that an overacting peristalsis is hastening to get rid of whatever the intestinal canal contains and the patient feels relieved when gas is passed through the rectum The more purging before operation, the more severe the pains after operation The solar plexus resents the insult and proceeds to take its revenge An enema at least 12 hours ahead is the best pre-operative resource and it is well known that emergency operations admitting of no preparation are followed by less pain than formal procedures with elaborate preparation All this seems to signify that stirring up the intestines beforehand and rendering the bowel too empty will cause the greatest hyperperistalsis after operative interference

Our object, then, is to encourage the normal peristaltic movement after abdominal

operations to regulate it, if feasible, not to hinder it. About 20 years ago my associates and myself devised a plan, followed more or less routinely ever since, to be used in every case when annoying peristaltic pain appears.

Of primary importance is the necessity of instructing nurses to recognize the "gas pains" in their very beginning, their fleeting character, their constant change of location, their association with waves of nausea. Success in their management depends chiefly on anticipating their development. The orders are a mustard plaster or hot camphor stupes, on the epigastrium, insertion of the rectal tube for 30 minutes, flushing the lower colon through the tube, in and out, with warm saline solution. In a half hour the tube is removed and 10 grains of quinine muriate in 8 ounces of water are injected slowly into the rectum. This is repeated in 4 hours. Generally relief is prompt, but if not complete, the same process is carried out again 6 hours afterward. No other measures are allowed to interfere with these orders, no fussing around to do this or that, until the results of the routine procedure are determined. If gaseous distention ensues, and the pain diminishes,  $1/40$  grain of eserine salicylate and  $1/60$  grain of strychnine sulphate are given hypodermically every 3 hours for 3 doses, followed by an alum enema (1 ounce to the quart of warm water) 1 hour after the last dose. On the contrary, if the pain increases with little or no distention,  $1/100$  grain of hyoscinæ hydrobromate and  $1/12$  grain of morphine sulphate are given hypodermically 1 dose, followed by the alum enema 1 hour later. These accessory orders are seldom needed in the ordinary case for under the three steps first mentioned, flatus is passed, not infrequently small fecal results are obtained and by the end of the second day the patient is comfortable. Persistence of slight pains may be relieved by  $1/2$  grain of pheno-

barbital, given every 4 hours by the mouth, continued for 2 or 3 days longer.

It might be well to consider the rationale of using the quinine injection. In my student days H. C. Wood taught that quinine stimulated the inhibitory center of the spinal cord. That recollection prompted the use of the most soluble salt of quinine for slowing peristaltic action after mechanical means had been employed to stimulate the activity of the lower bowel. Knowing that the older conceptions of the physiological action of many drugs had been superseded by later researches of modern pharmacologists, I recently asked William deB. MacNider of the University of North Carolina, to express his views upon the action of quinine for the purpose intended. In a personal communication, he replied:

My feeling is that the quinine muriate could act in a variety of ways on the intestine to cause the passage of accumulations of gas. 1. The first place it could act directly on the involuntary muscle tissue of the intestine. In very weak dilutions quinine tends to stimulate this type of tissue. On the other hand, it could influence the passage of gas through the intestine by its action on the central nervous system, either by stimulating the motor nervous mechanism to the intestine which is the vagus nerve, or it might relax the intestine and permit the passage of gas by stimulating the inhibitory nervous mechanism to the intestine which is, of course, furnished by the sympathetic system.

It is hardly necessary but perhaps excusable, to mention that the most effective way to prevent "gas pains" is to refrain from adding insult to injury inside the abdomen, to handle the parts politely, to avoid evisceration as far as permissible, to get in and get out safely, swiftly and sweetly, to forsake the ponderous pounding of the "abdominal brain" and to cleave only unto a gentle attention to the lesions at hand. By giving heed to these observances we may bring hundreds of patients through to convalescence without gas pains, without anodynæ, without meddling of any sort. HUBERT A. ROYSTER

# LANDMARKS IN SURGERY

## ILIAC COLOSTOMY

R W McNEALY, M D, F.A.C.S., AND MANUEL E LICHTENSTEIN, M D, F.A.C.S., CHICAGO, ILLINOIS  
From the Department of Surgery Northwestern University Medical School

THE first record of colostomy in the modern sense is the suggestion by Littre that the operation be performed for obstruction of the rectum. In *Histoire de l'Académie Royale des Sciences* (1710) under the heading "Diverse Observations Anatomique" (p 36) Fontenelle, secretary of the Royal Academy of Science, records that in the body of an infant that died 6 days after birth Littre saw the rectum divided into two parts which did not communicate with each other except by several small bands. It appeared that a part of the rectum had not developed in proportion to the rest of the intestinal canal. As a consequence these parts tore loose from the undeveloped portion and became entirely detached except for the few bands which held them together. Later the upper part of the intestine became filled with meconium while the lower part remained empty. One can see what might follow such an anomaly and how the death of the child would be prompt since its excrement could not be evacuated and whatever might be given to accomplish this would tend to aggravate this condition. The report continues:

M. Littre who wished to make his observation useful imagined and proposed a very delicate surgical operation for cases in which one would recognize a similar conformation. It would be necessary to make an incision into the abdomen, stitch together the two parts of the intestine after opening them, or at least bring the upper part of the intestine to the abdominal wall where it would never close and take on the function of an anus. On this simple idea clever surgeons could imagine for themselves the detail which we suppress. It often suffices to know in general that a thing may be possible and not to despair of it at first sight.

In this paragraph there is the suggestion that entero anastomosis be performed as the operation of choice for sidetracking an obstructive lesion in the bowel. If this is not possible, he suggests as a last resort, that a permanent colostomy be established. There is no record that Littre himself performed this operation. However, in the subsequent literature on colostomy, the left iliac colostomy has been called the operation of Littre.

Alexis Littre (1658-1725) was one of the gross anatomists who lived in the transition period of the 17th and 18th centuries. As the 17th century was notable for the many anatomical discoveries associated with the names of Bartholinus, Wirsung, Highmore, Glisson, Wharton, Willis, Havers, Cowper, Malpighi, Pacchioni, Meibom, Brunner, DeGraaf, Buck, Stenson, Peyr, and others, so the 18th

century was notable for the anatomist-surgeons who stood out prominently for their ability to make use of their knowledge of anatomy in clinical surgery. Hunter, Camper, Scarpa, Petit, Anel, Brasdor, Bichat, Chopart, Heister, Pott, Cooper, and Abernethy are some of these anatomist-surgeons. Littre made a study of the anatomy of the urethra and the urethral glands (glands of Littre, 1700) and described a type of hernia (Littre hernia, 1714). His observations concerning anatomy, made with a view of surgical application anticipated the advent of the master surgeons whose backgrounds were to be wholesome knowledge of anatomy.

Historically, the record of the first colostomy actually performed in 1776 by Pillore was not available in the literature until 1840. On January 14, 1840, in *Gazette des hôpitaux*, vol. 13, 2nd series No. 2, p. 22, there is published a letter which states in part,

In all the surgical works which speak of the procedures and methods in use for establishing an artificial anus after having described the procedure proposed by Littre narrate that Duret (of Lyon) and Pillore (of Rouen) have established with success an artificial anus in the adult. It is in *Mémoires de la Société de Médecine de Paris* that one is able to read the details of the operation of Duret, but one is nowhere able to find the description of the operation of Pillore (of Rouen) also it was in vain that Dupuytren begged me to show him where this had been published. M. Velpeau was not very happy when he asked for the same information from my son, then an interne in his service.

On the 16th of last November M. Amussat wrote my son a letter in which he asked of him again for this observation. He begged him to let him know if he was able to find out something about the known facts and continues as follows: "Pillore (of Rouen) appears to be the first who had practiced the procedure of Littre. Martin, the younger, in a report which he made to the Society of Medicine of Lyon, 1798 after having narrated the facts of Duret, said p. 189 of the report of the acts of the society.

Pillore, surgeon of Rouen, disciple and contemporary of Lecat, has carried this out successfully but his incision, made in the right iliac region gave access to the cul-de-sac of the cæcum."

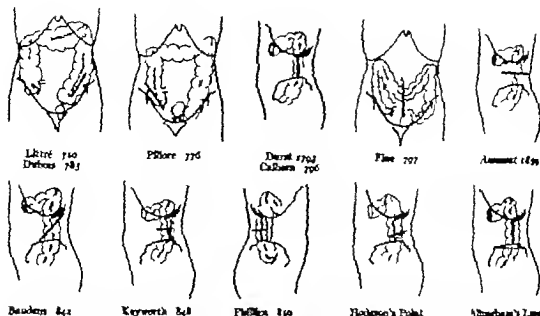
"Fine surgeon in chief of the hospital in Geneva, says in a memoir on artificial anus that he had published in the year 13 (1805) in the *Annals of the Medical Society of Montpellier* the following:

"(I have unsuccessfully asked and made request of M. Pillore, the father very advanced in age and since his death of his son a surgeon at Rouen, the information concerning when this operation was done, on the case which required it, on the manner in which it was carried out, and also on what the results have been. I hoped that the observation may be found in the papers of the deceased. It is to be regretted that operative medicine should be deprived of the details of an operation which presents great interest and on which Mr. Martin had only a 'hearsay knowledge'. )

It was thus that on going through the papers of my father I found the observation which I give you.

Rouen January 5 1840 H. Pillore père D.M.





Littre suggested left iliac colostomy in 1811. DeBore performed this operation in 1883, but the patient died. Duret in 1793 performed the first successful operation. Pflore suggested and performed the first right iliac colostomy (cecostomy). Duret in 1793 practiced an exterior of an infant, lumbar approach to the colon for the purpose of reaching the peritoneal cavity. The peritoneal cavity was opened and this approach therefore was abandoned. Callens in 1796 advocated the lumbar approach for intestinal obstruction. Fine in 1797 attempted to relieve an intestinal obstruction by opening the ilium but a low lying transverse colon was opened in the midline below the umbilicus. This was the first recorded median colostomy. The danger of the abdominal approach because of peritonitis was too great in the increasing number

of cases of intestinal obstruction that demanded operation. Between 1776 and 1899, thirty three colostomies were reported and about 25 of the patients died. In 1899 carried out successfully the vertico-peritoneal approach to the colon in the lumbar region by means of transverse incision. Baudens in 1841 suggested an incision that was oblique in line with the vessels and nerves. Keyworth and Phillips made T-shaped sections to facilitate the exposure of the colon. In order that the colon could be properly located, Hodgson described point and later Alvingham in 1896 described line overlying the colon. This brought the incision operation to perfection but the advent of anastomotic and later anastomotic surgery resulted in the abandonment of this operation. With the increasing use of colostomy the approach of Littre became more popular.

Very often he replied, it is necessary to have recourse to the operation when it alone is able to save me. You agree that but my chance is mortal.

Encouraged by these very good reasons, I performed the operation in the presence of my confederates, and of an immense people who were with me then. I chose the incision at that part of the lateral wall suited to our need, so much by its situation as by its ease it would furnish recovery, and by its continued and its voluntary action would hasten the structure of the intestinal contents. A plate furnished with openings in the shape of letters and held by an elastic bandage took the place of splint which would be removed at will when he felt the need and by means of small cylinders he could from time to time cleanse out the passage. My patient and I conferred together and thought of all these things before the operation. I then operated.

The operation consisted of exposing the cecum, opening it and returning its edges to abdominal wall.

The patient improved considerably and his abdomen decreased in size. However the mercury blick had been taken months previously had not been expelled. The patient was put in various positions to facilitate its passage but without avail. After a weeks the patient developed pain in the abdomen. On the twentieth day his abdomen became distended

Following this appears the case report. It is apparent from this letter that many are interested in the facts regarding this case. It was the first deliberate operation on the colon for relief of obstruction and, contrary to the suggestion of Littre, it was performed in the right lower quadrant of the abdomen. However there is no evidence that Pflore was familiar with Littre's observation.

Briefly the patient had been obstructed for a month during which time he was unable to evacuate his bowels. He had taken pounds of mercury without any effect on the obstruction. Rectal examination showed tumor mass that was responsible for the obstruction. As no relief could be obtained by the use of rectal dilators, Pflore proposed that an artificial anus be made. He continues:

I was then asked determined to perform the operation but as the case was very delicate and I asked five or six of my colleagues to see the patient in consultation with me. No one was of my opinion, but the patient, such of great anxiety present at our consultation begged them to show him any other means by which he might be saved. They answered that they knew of none.

and tender and in spite of emollient fomentations, enemas through the artificial anus and two bleedings, the patient died on the twenty-eighth day.

At autopsy it was found that the cecum was adherent to the edge of the wound except in one angle where there was a small area of suppurative which did not communicate with the peritoneal cavity. The cancerous obstruction which was the primary illness was situated at the rectosigmoid junction and completely occluded the lumen.

The peritoneal cavity was inflamed and adhered to the folds of the intestines. The mercury which the patient had taken was found in one of the loops of the jejunum which it had dragged down by its weight to the hypogastrium behind the bladder. This loop of bowel had several gangrenous areas. All of the mercury was recovered. Pillore continues:

We believe that we could conclude that if the operation has not met our expectations for its success it was because of the mercury. For it is very probable that when the intestines which because of their great dilatation had lost their power of action became empty of stercoral material peristaltic action was not sufficiently powerful to move the mercury. Then followed inverted and retrograde movements as announced by the nausea and colic which the patient experienced on the twentieth day of his illness. Considering the pull on the mesentery and intestines by this mass which weighed two pounds one is not surprised at the gangrenous inflammation which produced the death of the patient.

In 1783 Dubois performed Littré's operation on a three day old infant born with an imperforate anus. The child died on the tenth day. The autopsy showed consolidation of the walls of the rectum which produced obstruction. This case was mentioned by Allen in 1797 in *Recueil de Médecine*, Paris, 3, 123, who stated that he had information that Dubois was the first to practice what Littré had proposed.

The first successful left iliac colostomy (Littré) was performed by Duret in 1793. The case was reported by Duret in *Recueil de Médecine* Paris, 1798, 4, 45. It concerned an infant born with a maldevelopment of the scrotum and perineum. There was an anus but no rectum appeared to be present. A consultation of the physicians and surgeons on the staffs of the various hospitals at Brest was called. After efforts to establish a vent by probing through the site of the anus proved useless this means of therapy was abandoned. About a day and a half after birth a second consultation was held. It was decided to make an artificial anus. In an effort to expose the colon without opening the peritoneal cavity, Duret practiced a lumbar operation on a new born who had died 15 days after birth. This procedure was not successful as the peritoneal cavity was readily opened. Duret continued:

This case ended after this trial having prolonged the discussion sufficiently to prove its interest to humanity and honor to surgery. I decided (1) that without extraordinary means the loss of the child was inevitable. (2) that the axiom of Celsus that it is better to employ a doubtful remedy than to allow the patient to certain death here found its application. (3) that the decisions of M. Hevyn upon laparotomy were not contradicted

by this operation since the cause and course of the malady were as here recognized. I opened the belly of the little patient in the iliac region in the neighborhood where the sigmoid colon was forming a tumor a little apparent and where the meconium already imparted a deeper color to the skin. I made an opening about 20 inch and a half long which served for me to introduce the index finger into the belly, with which I lifted and pulled out the sigmoid colon. In the fear that it would immediately fall back into the belly I passed two waxed threads through the mesocolon. I then opened the colon longitudinally. Gas and meconium came out in abundance. When the bowel had emptied itself to a certain extent I applied a dressing. It was simple and was composed of a pierced compress and a body bandage.

The patient recovered from the operation and lived 43 years. Death was reported due to an intercurrent infection.

In 1795, Daguesseau performed Littré's operation for perforation of abdomen with injury to bowel.

In August 1795, 57 during harvest, occupied in loading his cart with wheat during an effort to lift a sheaf the band having broken he lost his equilibrium fell and the left side of his abdomen struck one of the stakes forming the side of the cart with sufficient force to cause it to penetrate deeply. Taken home M. Daguesseau a surgeon residing at Chadurec, was called to him immediately and decided upon establishing an artificial anus according to Littré's method. No consecutive accidents occurred and the patient soon got well and lived 24 years for he died in 1810 aged 81. A small leather sac was adapted to the opening by Daguesseau to receive the feces.

The use of the leather colostomy bag was thus established.

Dufresne, who reported the above case in *The Medical Times*, 1840, 10, 446, remarks:

This case, though incomplete is interesting because at the period at which the operation was performed only one case had succeeded—that of Duret of Brest in 1795. The patient operated on by (Pillore) in 1776 died 28 days after that by Votaire Dubois on the tenth day and that by Desault likewise died.

In 1811, Daguesseau performed Littré's operation for fistula in ano, with a successful result. The details of this case are as follows:

Masset a potter at St Eutrope was affected with several *hs ulæ in-ano* and having consulted Daguesseau this practitioner considered it impossible to obtain a radical cure except by establishing an artificial anus in the left hypochondrium according to Littré's method. This operation performed in 1811 succeeded the fistula canalized after which the artificial opening gradually diminished in size and in years was completely closed. The cicatrix from an excess committed by the patient burst open notwithstanding the presence of a truss but by appropriate remedies and rest, it healed once more and the man was thus delivered of the two infirmities.

Dufresne who reported this case also in 1840 says:

This case which has no precedent in its favor may astonish some persons and the operation be considered as not indicated; all that can be said is that Daguesseau's talent was sufficient to enable him to form an opinion as to the absolute necessity of the operation here performed.

These brief abstracts of case reports and quotations from the literature of a century and more ago demonstrate the ingenuity of the anatomists and surgeons who conceived and developed this important operation.

# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

*THE Woman Asks the Doctor*<sup>1</sup> is a remarkably clear and simple "exposition of the special problems in the every day living of women." Its authentic simplicity should counteract much of the pseudo-science that has flooded the market in recent years in response to the very evident desire which women are showing to know more about their physical beings. This desire has long been sensed by the quack and the charlatan; physicians have usually recognized it only when appealed to in individual instances.

It is gratifying to read Dr. Novak's dedication "To woman the Socratic injunction to 'know thyself' has peculiar force and significance. To know or not to know often means the difference between happiness and misery; mental and physical sickness and health, even life and death."

The book is a splendid and rational explanation, toned down to reach the lay mind without "talking down." It presupposes a certain intelligent conception of the fundamentals of life and explains many of the doubts and difficulties that confront the average girl or woman. Especially commendable are the chapters on menstruation, the menopause, and marriage. The chapter on "Sex" leaves much to be desired. The author states that he has no interest in generalising on this subject, believing that sex is always an individual problem.

This is a valuable addition to every physician's library for not only should the physician read this volume, but he should also recommend it heartily to those of his patients who are seeking knowledge.

RALPH A. RICE.

*THE* fourth edition of the well known Eden and Lockyer *Gynaecology*<sup>2</sup> has been most ably edited by H. Beckwith Wilks. A number of new chapters have been added, viz. the physiology of the female sex organs, gynecological diagnosis, contraception, etc. The chapters on the pathology of the endometrium and on ovarian disease have been completely rewritten.

The last third of this large volume is devoted to surgery. It is most complete, well illustrated, and

THE WOMAN ASKS THE DOCTOR. By Ewald Novak, M.D. F.A.C.S. Baltimore: W. B. Saunders Co. 1923.

GYNÆCOLOGY, PHYSIOLOGY AND PATHOLOGY. By T. W. Eden, M.D., C.M. (Eden), F.R.C. (Eden), F.C.S. (Eden), F.C.O. (Eden), and Constance Lockyer, M.D. 8th (London), F.R.C.P. (London), F.R.C.S. (London), F.C.O. (London), ed. by H. Beckwith Wilks, M.B., M.D. (London), C.M. (Oxford), F.R.C. (Oxford), F.C.O. (Oxford). London: J. & A. Churchill, Ltd. 1923.

most inclusive, containing as it does all of the accepted gynecological procedures in use today. The section on gynecological diagnosis and treatment is also most excellent. It contains a splendid differential diagnosis for each condition together with an adequate discussion of the various methods of treatment.

It is most pleasing to read the new chapter which has been added on contraception. It is short but complete, discussing all of the various contraceptive methods and devices. This subject belongs in a modern work on gynecology and it is unfortunate that the vast majority of authors continue to omit the topic completely.

The many illustrations are worthy of comment, especially the many excellent color plates which are found throughout the book. This volume is to be recommended most heartily. It is the most complete one volume work on the subject in the English language and should be found in the library of every physician who is interested in the subject of gynecology.

RAUL A. RICE.

*THE* twelfth and last edition of Osler's classic<sup>3</sup> was revised and edited by the late Dr. McCrea. The revision has been thorough and complete. The type used is easily readable but allows more words per page than decreasing the size of the book. The general outline of Osler's original volume has been followed. Attention is made of new thought and procedure, but the text is characteristically conservative. There is very little discussion of theory. The chief alterations have been made in diagnosis and therapy. New conditions are described and diseases which have recently become of particular interest receive special attention. There is practically an entire new discussion on such diseases as subacute fever, chronic hyperassutism, digestive disturbances due to food allergy, the anemias, certain phases of heart disease, subarachnoid hemorrhage, and countless others. The section on diabetes mellitus has received particular attention and new food tables are included. This work, always an outstanding text book, has been brought up to date and should be a valuable addition to every doctor's library.

WILLIAM H. HICKMAN.

THE PRINCIPLES AND PRACTICE OF MEDICINE. By Dr. William Osler, M.D., F.R.S., and Thomas McCrea, M.D. 12th ed. New York and London: D. Appleton-Century Co. 1923.

# SURGERY, GYNECOLOGY AND OBSTETRICS

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## THE FREE TRANSPLANTATION OF SKIN

### AN EVALUATION OF METHODS<sup>1</sup>

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THE transplantation of skin by means of pedicled flaps was a well known practice centuries before the development of early European surgery. Among the earliest procedures are those known as the "Indian" method, and the "Italian" method, both of which were used principally in the restoration of the nose or other parts of the face which had been amputated by enemy peoples. Although countless modifications of these principles were made over a period of many years, one of the most important improvements in the transplantation of skin by the pedicle method was developed by Gillies (10), who, after undermining between parallel incisions rolled his skin into a tube, held so by suture of the edges. This principle was described by Filatoff prior to Gillies' publication of the method but has become known since as the Gillies tube method of skin transplantation and together with the Indian and Italian methods, has been proved to be a sound practical method of pedunculated skin transplant.

In contrast to the pedicle principle, the free transplantation of skin implies the excision of a portion of skin and transference of this graft to another portion of the body, its viability depending upon immediate fixation to the underlying tissue and the rapid establishment of a capillary blood supply. The development of this method of skin transplantation belongs

to a relatively modern period in comparison with the antiquity of the pedicle flap types.

Because of the tendency for most writers unconsciously to favor the particular type of skin graft with the development of which they have been concerned, it is perhaps justifiable for one who has fostered no new ideas relative to the subject, but who has tried to profit by the best in each, to criticize the most common present day methods of free skin grafts.

Reverdin is generally credited with the first successful demonstration of the transplantation of small bits of skin from a remote part of the body applied to a granulating surface. Epithelization of the defect was seen to follow the application of these small grafts which were epithelial islands proliferating at the borders and ultimately coalescing. In addition to the importance of Reverdin's work as being the first practical method of free skin grafting it is of considerable interest that his favorable results were obtained before the era of antiseptic and aseptic surgery. First thought to be grafts of epidermis only, Reverdin later recognized that his grafts contained a portion of the corium.

Davis (5) in 1914 first described the "small deep graft" and has reported its use in several communications since that time (6, 7). In principle, there is little to differentiate it from the "pinch grafts" of Reverdin except that a

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greater portion of corium is removed with the central portion of the Davis graft and further that the bit of skin to be removed is raised with a needle rather than being "pinched" upward into a tented contour by forceps. The grafts are placed at some distance from each other upon a granulating area and in both the Reverdin and Davis procedures healing depends upon the eventual coalition of these small epithelial islands.

The value of this type of graft is indisputable for the repair of large defects where the donor areas are relatively limited and where safety to the patient demands a minor surgical procedure. Because of the simplicity of the method and the assurance of a high percentage of "takes" even upon grossly infected granulations, these small grafts have become widely popular and each year a great many burned children are rehabilitated by the use of this type of graft only.

There are, however, several definite objections common both to the pinch graft and the deeper graft of the same size among the most important of which is the appearance of the grafted area after healing is complete (Fig. 1). Because the central portions of the grafts include a thickness of corium not present at the edges nor in the spaces between the grafts, an uneven, mottled surface results which has an unpleasant appearance particularly on exposed body surfaces. The same objection applies to the donor areas, which are usually the thighs, and which have an unsightly appearance after healing has occurred.

Owing to the fact that these small grafts are generally placed upon old granulations and that some time must elapse before they proliferate sufficiently to cover the defect it is inevitable that some of this granulation tissue must remain permanently as undesirable scar under and between the small epithelial islands. Needless to say, if there is a tendency toward keloid formation the use of this type of graft is highly unsatisfactory.

After an experience of several years Thiersch in 1886 reported on a method for the grafting of large sheets of partial thickness of skin which included a portion of the corium. Although Lawson and Ollier had both used this method prior to the work of Thiersch,

the latter's name is usually applied to this type of graft. It marked a distinct advance over the small pinch grafts of Reverdin, since much larger areas were covered in one procedure and it is probable that this type of free skin graft has enjoyed a greater popularity and served a broader field of usefulness than any other to a most recent period.

These larger than split sheets of skin have in addition to many of the desirable features of the small grafts of Reverdin and Davis, relatively few objectionable characteristics. Where adequate donor areas are available sizeable defects may be covered in one operation with a fair expectancy of take even upon an infected surface. Because of the greater size of the individual grafts, which vary depending upon the donor areas available and the dexterity of the operator there is less chance for the formation of scar between grafts than in the smaller variety and the final appearance of several large sheets of grafts is usually better than that of an area covered by a great many small coalescing islands of epithelium. If care is exercised in cutting Thiersch grafts not to incise into the subcutaneous fat spontaneous regeneration of the entire donor site will rapidly take place and the area will eventually assume the appearance and texture of the surrounding skin. Reference to this regeneration will be made later.

It should be mentioned, however, in a fair criticism of the Thiersch graft that it includes, in most cases, only a small portion of the corium removed with the epidermis which at best provides a poor foundation for epithelium and in areas subject to pressure or friction may provide quite inadequate protection for the underlying tissue. Considering also the great thickness of elastic corium in normal skin it may also be anticipated that considerable contraction will occur under a graft having for its anchorage the thin portion of corium usually found in a Thiersch graft.

The first use of a full thickness free skin graft is generally conceded to Wolfe of Glasgow who in 1873 reported the repair of a defect about the eye by this method. Although other workers undoubtedly deserve credit for the development of this type of fat free full



Fig. 2 a. Removal of thick split graft from the thigh. The suction retractor designed by Blair precedes the course of the knife and maintains an even tension of the donor area. The tongue blade, held by an assistant, should be advanced behind the knife. Such large grafts are to be re-



moved. b. A sizeable graft of uniform thickness ready for removal and application to the denuded area. A larger graft could have been removed without difficulty, but measurement of the defect made previously showed it to be adequate.

closure, since the entire thickness of skin has been removed.

For a number of years, Blair and Brown (1) have been advocating the use of large free split thickness grafts in the repair of extensive cutaneous defects. They have suggested the term "thick split graft" (since it includes one half to three-quarters of the thickness of skin) to differentiate it from the thinner Ollier Thiersch graft and also from the full thickness Wolfe graft. Their technique for the removal and application of these grafts has been adequately described in several publications (2, 3, 4) and requires no amplification. In principle, these thick split grafts are quite similar to Ollier Thiersch grafts, except that very much larger individual grafts are cut

the area to be grafted is specially prepared and the application and fixation of the grafts differs from that commonly employed in the use of the Ollier Thiersch grafts.

These large split thickness grafts have, according to Blair and Brown, more of the good than the bad features of either the full thickness graft or the thinner Ollier Thiersch graft. The writer's experience of several years unqualifiedly supports their opinion.

By the use of a suction retractor and a specially constructed knife described by Blair (1) in 1939, large individual grafts of uniform thickness 25 to 50 square inches may be cut from suitable areas (Fig. 2). Often a single graft is sufficient to cover the defect and if not, the adjacent edges of the grafts are su-

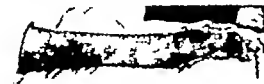


Fig. 3 a. Gasoline burn of 6 months' duration. The portion of the hand not denuded is covered by thin and quite unconvincible epithelium on scar base. The graft on the forearm as done 3 weeks prior to this photograph. b, 1 he scar and granulations down to tendon sheaths



by sharp dissection. The bleeding is usually controlled temporarily by hot packs and pressure, although the applications of the graft act as an excellent hemostatic. c. Application of the graft. Allowance is made for some over-lapping of the graft at the edges of the defects and accurate approximation is effected by continuous sutureless nature of low air or some compressible material. Multiple perforations are made in the graft to permit the escape of serum and blood, and pressure dressing is applied after the careful removal of clots from beneath the graft. Although unnecessary in this instance, pressure over surfaces on the trunk or in situations such as the axilla is best maintained by the use of large sea sponges. Such are restrained below they are used.



a

Fig. 4. a, Appearance of the hand shown in figure 3 3 weeks after grafting. The careful suturing of the graft edges produces only a minimal linear scar which becomes almost obliterated in time. Motion of the fingers is limited



b

by scar and damage to joints themselves, but the tendons move freely without fixation under the graft. b Volar aspect of the same extremity. The single graft on the fore arm was done 5 weeks prior to this photograph.

tured together producing only a linear scar. Because of the size of these grafts, surfaces 100 square inches or more may easily be covered in one procedure.

The thickness of the grafts varies somewhat, depending upon the age and sex of the patient, as well as the location of the donor area, but in general, one-third to three-quarters of the thickness of the corium is included with the epidermis. This in most cases, is a depth great enough to provide the graft with accessory skin structures, and the end-result is a durable covering containing hairs, sebaceous and sweat glands, and closely resembles full thickness skin. Although this graft may prove impractical in a location subject to great friction or actual weight bearing, it may be of great value as a temporary covering for such a granulating area, preliminary to an eventual full thickness graft of some variety.

Preparation of a granulating area to be grafted includes, in addition to the usual measures to minimize infection (1) excision of the scarred border of the defect and (2) slicing off of the superficial edematous granulations together with some of the underlying scar until a firm scar base is reached (Fig. 3). This preparation, together with adequate provision for drainage by perforations in the graft, and careful fixation of the graft with suture and a pressure dressing, by means of a marine sponge, assures one of almost 100 per cent "take" in the great majority of cases. The first postoperative dressing may be done at any time after 3 or 4 days when the grafts will usually be found to be firmly grown to the underlying scar and to require little or no further attention (Fig. 4).

Healing of the donor areas from which these large thick split grafts are removed, is of some interest, since if one is careful to avoid cutting into the subcutaneous fat, spontaneous regeneration of even very large areas will occur within a week to 10 days. Covering of these areas with a tannic acid crust is a satisfactory dressing though probably less comfortable than a firmly applied gauze dressing left unchanged for 7 to 10 days.

Regeneration of an intact epidermis after the removal of an Ollier-Thiersch graft was formerly thought to be from the deepest portions of the papillary layer of the epidermis left below the level at which the graft was taken. With the demonstration that thick split grafts included in addition to the entire epidermis enough corium to remove hair bulbs situated deep in the true skin, it was apparent that an entirely new epidermis must regenerate from structures in the remaining thinned-out dermis (Fig. 5). Biopsies removed from the donor site on a thigh at the time of removal of the graft and 3, 6, and 10 days later, show without question that the regeneration of the new epidermis is from the hair follicles and associated sebaceous glands, and that within the 10 day period, a complete new epidermis has been formed, differing in some respects from the previous one but having very active growth and well differentiated cellular layers (Figs. 6, 7, 8, 9).

This mode of regeneration is not surprising when one considers that the hair follicles are embryologically invaginations of epidermis and that the outer root sheath of the follicle is a direct continuation of the stratum germinativum of the epidermis. Since it is also



Fig 5



Fig 6



Fig 7



Fig 8



Fig 9

Fig 5 Low power photomicrograph of thick split graft (above) and higher power of sections of the remaining corneal and substantia propria tissue, removed immediately after the graft was cut. The graft includes, in addition to the entire epidermis, an appreciable portion of cornea, although less than is usually reserved. Note the obliquely cut hair follicle on the denuded surface of the donor area.

Fig 6 Biopsy of donor site 3 days after removal of thick split graft. Photomicrograph of section cut at right angles to the denuded surface, passing obliquely through two hair follicles. A single layer of columnar cells, deeply stained and continuous with the outer root sheath of the hair follicle, is seen extending over the surface of the cornea. Immediately above the mouths of the follicles, additional layers are seen, which have become stratified, squamous epithelium. A marked inflammatory reaction is seen throughout the cornea.

Fig 7 Biopsy of the donor area immediately adjacent to that shown in Figure 6, 6 days after removal of graft. The source of the new stratum germinativum from the outer root sheath of the hair follicle is more clearly shown, with an exaggerated thickness of the new epidermis in the immediate vicinity of the follicle. The stratified squamous character of the upper layers is seen, with beginning cornification and desquamation of the surface layers beneath the blood and debris.

Fig 8 Section of biopsy taken from the area adjacent to that shown in Figures 6 and 7, 7 days after removal of graft. An entirely new epidermis has regenerated over the surface of the cornea, having more mature characteristics and greatest thickness near the hair follicle.



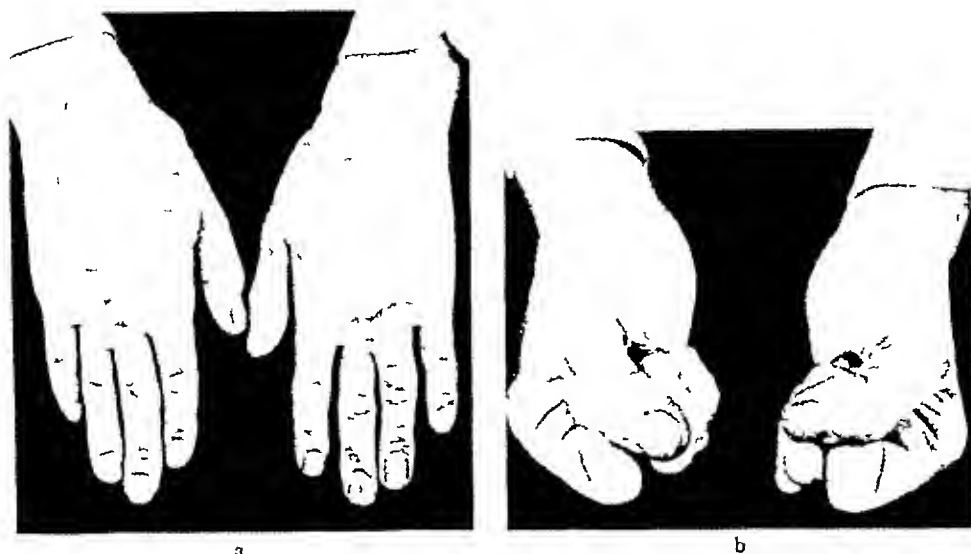


Fig. 10 a, Burns of hands 19 years previously. X ray treatments for scar resulted in radiodermatitis with carcinomatous change on the dorsum of both hands. The lesion on the right had been excised and the defect repaired by a pedicle flap. We excised a carcinoma 3.5 centimeters in diameter from the left hand and used a thick split graft for repair. There was no recurrence or metastasis in 1½ years. We favor, as does the patient, the end result on the left hand from the standpoint of appearance, function and loss of time involved. b, Function of both hands equally satisfactory.

true that the actual number of hairs may increase during life by the development of new follicles after the manner of the primary formation (18) it is logical to expect that with the traumatic or surgical loss of the epidermis the process will be reversed with an upward growth of the outer root sheath of the hair follicles in the region and a fusion of these cellular outgrowths to form a new epidermis. This conception of epidermal repair may have some relation to the almost universal distribution of hair over the body surface and accentuation, with reference both to the number of hairs and coarse nature, over body surfaces commonly subject to trauma such as the dorsum of the hands and arms, legs and anterior aspect of the trunk. The rapid regeneration of a new epidermis from hair follicle proliferation seems less remarkable when one

considers the unusual growth properties of hair in general and particularly the beard of an adult male. There are probably few structures in the body capable of as active growth as that shown by hair.

The thick split graft has then in addition to others two decided advantages as compared with other types of free grafts since (1) the graft itself has many histological characteristics and the gross appearance of full thickness skin and (2) the large areas from which the grafts are cut regenerate spontaneously with a modified, but thoroughly serviceable type of epithelium.

#### SUMMARY

For the reasons enumerated in the discussion of the pinch and the small deep graft, we have restricted its use to cases, usually children with extensive burns in which the available donor areas are relatively limited and in which the poor condition of the patient permits only a minor surgical procedure to initiate repair. In this group of cases there is no doubt of its usefulness admitting at the same time its shortcomings.

Fig. 9 Low power photomicrograph of same section as in Figure 8. A comparison of the new epidermis with that removed with the graft shown in Figure 3 (same magnification) demonstrates a striking difference. The new is several times thicker due probably to the demand for epidermal repair or possibly because of the relative thinning of the corium a portion of which was removed with the graft.

Although the Wolfe, or full thickness free graft should be, theoretically an ideal type of skin transplant in many instances, we must agree with a recent statement by Gillies (11) that the standard of technique for a successful result demanded by this type of repair and its tendency to subsequent mild trophic disturbance, do not justify its use in place of more certain methods.

With reference to the tunnel or buried full thickness graft, the rather narrow scope of applicability has limited and probably will continue to limit its use with a corresponding popularity of other types.

Although it has been generally felt that the repair of defects in certain locations such as around joints or over movable structures as tendons, require full thickness skin we have found that the thick split grafts furnish an adequate covering in many instances and reduce substantially the long periods of hospitalization necessary for the use of full thickness free, pedicle or flap types of grafts (Fig 10).

In commenting upon the thick split graft, it should be mentioned that the successful removal of large grafts requires some degree of manual dexterity and above all a sharp knife. With practice however and the meticulous care of the knife that one gives to a razor surprisingly large grafts of uniform thickness may be removed easily and quickly. We feel that the suction retractors designed by Blair have been of inestimable help to us in cutting these grafts.

Several factors mentioned in the previous parts of this paper have influenced the trend of free skin grafting in our hands resulting in a much wider use of the thick split graft and a corresponding infrequent use of the Ollier Thiersch and the full thickness types of grafts. There are relatively few instances in which a very thin Thiersch graft is actually preferable to the thicker split graft one of these being in lining the orbit. Since the donor area heals with equal readiness, regardless of the surface area or the thickness of the graft provided

the knife passes continuously *through* rather than *beneath* the corium, our preference has shifted decidedly in favor of the thicker one. Most situations require for the ideal, a greater thickness of corium than is usually included with either type which recommends in many instances the thickest graft which can be cut without the removal of full thickness skin.

#### BIBLIOGRAPHY

- BLAIR, V. P. and BROWN, J. B. The use and uses of large split skin grafts of intermediate thickness. *Gynec & Obst.* 930, 40, 87-97.
- Idem. The early cure of burns and the repair of their defects. *J. Am. M. Ass.* 934, 63, 355, 359.
- BROWN, J. B. BLAIR, V. P. and HARRIS, W. G. The release of ankylosis and brachial plexus lesions. *Surg. Gynec & Obst.* 933, 56, 700-708.
- BROWN, J. B. and BLAIR, V. P. The repair of defects resulting from full thickness loss of skin from burns. *Surg. Gynec & Obst.* 935, 60, 270-280.
- D. VAN, J. S. The use of small deep skin grafts. *J. Am. M. Ass.* 914, 63, 905.
- Idem. The small deep graft. *Ann. Surg.* 939, 89, 903.
- Idem. The small deep graft. *Ann. Surg.* 939, 91, 933.
- EMERY, J. F. S. Island flaps. New York M. J. 9, 7, 66, 364.
- FLATOW, W. Plastic two round. *Amst. Med. Weekl.* 9, 7 (April 18) Nos. 4-5.
- GILLIES, H. D. Plastic surgery of facial burns. *Surg. Gynec & Obst.* 930, 30.
- Idem. The role of plastic surgery in burns due to corrosive rays and radium. *Ann. Surg.* 935, 99, 990-996.
- KELLY, R. VAN L. Ten years of the tunnel skin graft. *Ann. Surg.* 930, 9, 934, 936.
- LAWSON, C. On the transplantation of portions of skin for the closure of large granulating surfaces. *T. Clin. Soc. Lond.* 87, 4, 40.
- MARTIN, A. Tunnel skin grafting: new method of covering raw surfaces with pathelium. *Glasgow M. J.* 9, 2, 78, 85-90.
- MOMMSEN, L. Ueber Verpflanzung Thiersch'scher Epidermisstücke in die Mundhöhle. *Arch. f. Klin. Chir. Berl.* 9, 6, 108, 6.
- OLLIER. Greffen cutanées ou autoplastiques. *Bull. Acad. de med. Par.* 873, 48, 44.
- PARK, A. D. An improved method of skin grafting. *Ann. Surg.* 93, 75, 658.
- PETERSON, G. A. Human Anatomy vol. 2, 6th ed. p. 402. Philadelphia. J. B. Lippincott Co. 9, 5.
- REYNOLDS, J. L. Quoted by Davis, J. S. *Plastic Surgery* p. 6. Philadelphia. F. B. Rothman. Son & Co. 9, 9.
- THIERSCH, J. Ueber Hautverpflanzung. *Verhandl. d. deutsch. Gesellsch. f. Chir. 17 Congress.* 1864.
- WOLFE, J. R. A new method of performing plastic operations. *Brit. M. J.* 475, September 8, 350.

## BILIARY DYSSYNERGIA PHYSIOLOGICAL OBSTRUCTION OF THE COMMON BILE DUCT

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**D**ILATATION of the bile ducts and intrahepatic biliary radicals indicates an obstruction to the free flow of bile from the liver into the duodenum. Calculi, inflammatory reactions, strictures, neoplasms, kinks, and functional derangements of the choledochoduodenal-sphincteric mechanism are the most important obstructive agents. Considerable emphasis has always been placed on the organic obstructions of the common duct, but little attention has been paid to the physiological dysfunctions of the choledochal sphincter which are capable of producing an enormous dilatation of the entire biliary tract.

Many surgeons have encountered hepatic congestion, bile stasis, and dilatation of the "biliary tree" without being able to demonstrate pathological changes to account for the obstruction. Such was the experience of Krukenberg who in 1903 reported a case of "gall-stone colic" in which neither calculus nor infection was found. In 1909, Aschoff and Bacmeister described the "stasis gall bladder" which occurred in the absence of stones, inflammations, strictures, or kinks. As a result of physiological experiments which were predicated on the anatomical work of Oddi, Meltzer in 1917 suggested that a spasm or an increased tonus of the sphincter of Oddi might act as a mechanical impediment and produce biliary colic and icterus.

Schmieden in 1920 offered a new idea. He had, in several instances, encountered markedly distended but otherwise normal appearing gall bladders in which he felt the distention might be caused by a kink or anatomical defect at the junction of the cystic duct with the gall bladder. According to Ivy, this theory was quickly accepted but was later criticized because the hypothetical anatomical hindrance could not always be demonstrated.

In 1922, Berg continued the studies of Meltzer and Westphal and concluded that a functional derangement, particularly a spasm

of the sphincter of Oddi, could easily produce a chronic stasis of bile. Newman, Nuboer, Giordano, and Mann, each reported cases in which a hypertrophied sphincter of Oddi had resulted in an occlusion of the common bile duct. In 1933, Strauss et al. presented 22 cases of chronic bile retention in which duodenitis with inflammation of the ampulla of Vater seemed to be the sole cause of obstruction. During 1934, Ivy and Sandblom made an intensive study of the abnormal motor responses of the gall bladder and bile ducts. They concluded that a functional disorder of the choledochus resulted in the accumulation of bile. To differentiate this from other forms of bile stasis, they used the term "biliary dyskinesia," which we shall designate as biliary dyssynergia, a more descriptive term.

By means of direct roentgenographic visualization of the biliary tract with radiopaque oils, we have been able to demonstrate that an increased tonus or spasticity of the choledochoduodenal-sphincteric mechanism is capable of producing a mechanical obstruction, thus causing a retention of bile. These deductions were corroborated by operative exploration and are predicated on the following experimental investigation.

**CASE 1.** Mrs. O. M., housewife, aged 58 years, entered the hospital complaining of "heartburn." During the past 10 years she had suffered from recurrent attacks of indigestion, characterized by epigastric distress, belching of gas, passage of flatus, and abdominal cramps. The ingestion of fatty foods, cabbage, apples, or pork always initiated an attack. In the last 4 years she had had several paroxysms of gall stone colic without jaundice.

The patient appeared to be a well-nourished woman. The gall bladder could not be palpated but there was slight tenderness in the right subcostal area. The gall bladder concentrated the cholecystographic dye but it did not empty well following the fat meal. Several small circular shadows were seen which were thought to be gall stones. Jaundice was not a factor; the icteric index and van den Bergh reactions being normal.



Fig. Case. Note the marked dilatation of the bile ducts. An obstruction near the ampulla has prevented the lipiodine from entering the duodenum. Radiograms made 3 hours later indicated the pseudo-obstruction had disappeared for the lipiodine, as then in the jejunum. A spasm of the choledochal sphincter followed by relaxation offers probable explanation for this observation. (Unfortunately the 3 hour plate was destroyed.)

At operation the liver presented no abnormalities except a mild fibrosis of its capsule. The gall bladder was distended and contained several small stones. Its walls were thick, firm, and undurated. The cystic duct was small, pliable, and contained no calculi, but it was sharply kinked at its junction with the gall bladder. The walls of the common duct were slightly thickened but there was no evidence of dilatation, stones, or neoplasm. The pancreas was of normal size and consistency. Black, acid bile was aspirated from the gall bladder. It was apparent that the mechanical kink of the cystic duct had interfered with the emptying of the gall bladder, producing stasis, infection, and stone formation. In spite of the fact that the common duct appeared perfectly normal, we decided to explore it. A longitudinal incision permitted the escape of dark brown, tenacious bile laden with flakes of biliary pigments. Irrigation with physiological saline solution dislodged considerable amount of inspissated bile pigments and mucus. Exploration with scope and probe demonstrated a pseudo-obstruction at the intestinal orifice of the common duct. When, however, stronger pressure was exerted, the instruments suddenly slipped into the duodenum, indicating that the mechanical impediment had been overcome. It then occurred to us that this pseudo-obstruction might be due to a spasm of the common duct sphincter. A cholecystectomy was performed without any difficulty.

Twenty-four hours following operation, 4 cubic centimeters of lipiodine (Ciba) was injected into

the drainage tube and permitted to flow into the common duct. Roentgenographic studies disclosed pronounced dilatation of the entire biliary tree. The common duct measured 14 millimeters in diameter which was 34 times its normal size, while the right and left hepatic ducts were about 35 times larger than usual. The walls of the dilated ducts were smooth and regular in contour showing no evidence of stones, strictures, or neoplasms. The remnant of the old cystic duct was dilated so that it formed a small saccululation. Apparently there was some impediment at the ampulla for the lipiodine, a condition the bile ducts, none having escaped into the duodenum (Fig.).

A second roentgenogram taken 35 minutes later revealed the lipiodine to be retained in the bile ducts. After three hours, the radiopaque oil as seen to trickle into the duodenum. Evidently the temporary obstruction, spasm or spasm had momentarily disappeared, permitting the dilated bile ducts to eject their only content into the intestinal tract. Radiograms taken 48 hours after the primary injection exhibited a slight retention of lipiodol in the hepatic and common ducts.

It is to be remembered that before exploring the common duct it appeared to be fairly normal; however, the visualization studies demonstrated a distinct dilatation of the entire biliary tract. Perhaps such a distention is much more common than is customarily believed. The operative exploration of the choledochus disclosed what was thought to be a spasm and hypertrophy of the sphincteric mechanism. Roentgenograms confirmed this impression by showing that there was sufficient spasm of the sphincter to cause a retention of lipiodol and it required 3 hours time for the sphincterism to subside sufficiently to permit the oil to enter the duodenum. If this obstruction were caused by an inflammatory reaction of the ampulla and duodenal wall, as suggested by Strauss, then it should have persisted, exhibiting no periods of partial relaxation during which the lipiodol could escape into the bowel. Thus it would seem that the spastic sphincteric mechanism acts as a mechanical hindrance to the physiological flow of bile, producing an increased intraductal pressure with subsequent dilatation of the biliary radicals and ducts, causing a cholangiectasia and even hydrohepatosis.

Does the choledochal sphincter have sufficient contractile power to overcome the normal intrahepatic and intraductal secretory



Fig 2, left Case 2 Roentgenograms taken 5 minutes after injecting lipiodine in common duct. Note the marked dilatation of the large bile ducts. The oil had not entered the duodenum because of a choledochal obstruction near the ampulla. Was this a sphincterismus?

Fig 3 Case 2 Plate taken 30 minutes later showed the lipiodine to be in the intestinal tract. There was still a slight stasis of oil in the common duct. The obstructing mechanism (Fig 2) had completely disappeared, which suggested a relaxation of the choledochal sphincter

pressure and produce a chronic retention of the biliary products? Whitaker has demonstrated that bile enters the gall bladder by flowing up the cystic duct, but it does this only when the sphincter of Oddi is closed. The existence of this sphincter as an anatomical and physiological structure has been much discussed, and it is now generally accepted as being a functioning unit. Its physiological action has been demonstrated by Lueth, who by means of an ingenious apparatus measured the pressure gradients in the intramural part of the common bile duct and obtained positive evidence of its sphincteric action. He showed that the ampulla could be distended with perfusion fluid, indicating that the terminal part of the bile duct must be able to retain fluids under positive pressure. This confirmed the previous findings of McMaster and Elman who had measured the pressure in different parts of the extrahepatic biliary system by means of triple intubation. Judd and Mann, and later Lueth, proved that the sphincter action was not produced by the tone of the duodenal wall. Cole, and Elman and McMaster found that, in a dog, the sphincter could hold up bile in the common duct at a pressure of 100 millimeters of water while Judd and Mann found the ampulla able to

withstand a pressure of 600 to 675 millimeters of water. Whitaker cut the sphincter of Oddi and found that the pressure within the common bile duct fell to zero and that the gall bladder did not fill. Ivy and Sandblom believe that motor dysfunctions of the sphincter of Oddi are capable of producing bile stasis and simulate the syndrome cholecystitis and biliary colic.

Such physiological evidence confirms our observation that a spasm of the choledochal sphincter is capable of producing and does produce bile retention by interfering with the normal emptying of the extrahepatic ducts.

**CASE 2** Mrs L. L., housewife, aged 32 years, complained of recurrent attacks of severe biliary colic for the past 3 years. About 4 months prior to admission, a cholecystectomy was performed and the gall bladder was found to be filled with calculi. Two weeks after the operation, the colic-like pains associated with nausea, vomiting, and jaundice, recurred. Since then she has had several acute paroxysms.

She was a nervous, emaciated woman. No tenderness could be elicited in the right subcostal area. The liver was not enlarged and the kidneys were not palpable. Roentgenograms of the abdomen and retrograde pyelograms depicted a round stone lying at the level of the second lumbar vertebra external to the urinary system, hence it was thought to be in the common duct.



Fig. 4, left. Case 3. On the seventh postoperative day lipiodone was introduced into the cholecystostomy tube. Only a very small amount of the oil passed into the common duct for the cystic duct was practically occluded.

Fig. 5. Case 3. Six days later similar injection was made. The lipiodone outlined the gall bladder, cystic duct, and dilated bile ducts. There was a mechanical blockage at the lower end of the choledochus which caused retention of oil. Radiographic studies made 30 minutes later revealed relaxed sphincter of Oddi for the oil was flowing into the duodenum.

Upon opening the abdominal cavity, the liver capsule was found to be stretched, its white fibrous tissue. There was pronounced dilatation and enlargement of the common duct caused by a calculus obstruction in its retroduodenal portion. As soon as the choledochus was incised, clear dark brown bile escaped, exposing a large prurby granular stone which was removed by scoop. Instrumental and digital examination indicated that the common duct was patent. A definite impediment, however, as encountered at the intestinal orifice of the duct and moderately sustained pressure was required before the resisting force was suddenly overcome and the curved hemostat entered the duodenum. A No. 7 soft rubber catheter was anchored into the common duct for drainage.

Twenty-four hours following operation 45 cubic centimeters of lipiodone (Ciba) was injected into the common duct. The radiopaque oil demonstrated pronounced dilatation of the bile radicals. In fact, the persistent intraductal pressure had been so great that it had caused the stump of the cystic duct to form a small diverticulum. No organic lesion could be demonstrated but the lipiodone failed to flow into the duodenum (Fig. 4). Thirty minutes later the oil was seen to be in the upper jejunum (Fig. 5). What was this evanescent obstruction in the region of the ampulla of Vater? If stones, strictures, neoplasms, or inflammatory reactions should cause permanent blockade but had that the apparent obstacle had disappeared within 3 minutes time permitting complete restoration of the biliary tree certainly could suggest a functional derangement of the sphincter of Oddi.

One naturally wonders whether there is a causal relationship between the motor dysfunctions of the choledochal sphincter and the presence of stones and infection. It is conceivable that an inflammation of the ampulla and the duodenum might occasionally increase the hypersensitivity of the sphincter and induce a spasm. On the other hand a primary sphincterismus could easily cause a retention of bile and stagnant bile on becoming infected would favor the formation of stones. It was impossible to determine whether the stone or the spasm of the sphincter was the provocative agent in this particular case. Undoubtedly most of the patient's symptoms were caused by the stone in the common duct but after the calculus had been removed the bile stasis still persisted because the abnormal physiological tones of the choledochal sphincter prevented the bile from entering the intestinal tract. Our experience with 7 other cases clearly demonstrates that it is possible for the common duct sphincter to function normally in the presence of generalized inflammation of the biliary tract associated with stones, strictures, and even a pancreatitis. This conception agrees with the observation of Sarazlegui who injected lipiodol into persistent external biliary fistulae of cholecystecto-



Fig 6

Fig 6 Case 4. On the fifth postoperative day, 40 cubic centimeters of lipiodine was introduced into the common duct. Note the extensive dilatation of the bile ducts. Roentgenograms taken 3 minutes after the injection of the oil demonstrated a blockade at the lower end of the choledochus.



Fig 7

Fig 7 Case 4. Second roentgenogram taken 10 minutes later. The obstruction was beginning to disappear as the oil was now slowly trickling into the duodenum.



Fig 8

Fig 8 Case 4. Studies made on the ninth postoperative day, 35 minutes after the original injection. The common duct was beginning to empty more rapidly. It required 1 hour's time for all the oil to enter the duodenum and yet no obstructive agent could be demonstrated at the operating table. An evanescent obstruction that completely occludes the common bile duct and then suddenly disappears seems to be suggestive of a choledochal sphincterismus.

mized individuals. He encountered considerable difficulty in visualizing the biliary tract because the radiopaque oil entered the common duct and immediately passed through the relaxed sphincter of Oddi into the duodenal lumen. Infection then does not necessarily cause a sphincterismus.

**CASE 3** Two weeks ago, Mrs. A. C., housewife aged 43 years, had her first attack of "gall stone trouble." It was characterized by a severe colic like pain most intense in the right subcostal area and radiating to the interscapular region. One week later, a firm tender mass could be felt in the right upper quadrant. The liver and spleen were not palpable but the abdominal muscles were slightly spastic. Her skin and sclerae were deeply jaundiced, the icteric index being 88. Roentgenograms demonstrated a non functioning gall bladder without evidence of stone formation.

Upon exposure of the gall bladder, it was found to be about three times normal size and to contain several stones. Its walls were acutely inflamed, thickened, and indurated. The serosa was studded by small petechial hemorrhages. The common duct was dilated and its fibrosed walls were firmly adherent to the duodenum and the fundus of the gall bladder. A large stone blocked the choledochal lumen. Sixty cubic centimeters of a thick, yellow,

purulent bile was aspirated from the gall bladder, thus confirming the diagnosis of acute cholecystitis. The calculi were removed from the gall bladder, and the cystic duct was found to be completely occluded by the inflammatory swelling and edema. The dilated common duct was opened and the single calculus removed. The pancreas and ampulla of Vater were normal. Scoops, probes, and irrigating



Fig 9 Case 5. Eight days following removal of an acutely inflamed gall bladder, 40 cubic centimeters of lipiodine was injected into the common duct via the cystic duct. There was no evidence of bile stasis or dilatation of the ducts. The choledochal sphincter was relaxed for the oil immediately entered the duodenum.



Fig. 3

Fig. 3. Case 6. Visualization studies on the twelfth postoperative day disclosed retained choledochal sphincter for the oil passed unabsorbed into the duodenum. The common duct was dilated. The finer biliary radicles did not visualize because ascending cholangitis had plugged the smaller ducts and because the relaxed sphincter permitted the oil to escape.



Fig. 4

Fig. 4. Case 6. On the twenty-fourth postoperative day



Fig. 5

the finer bile ducts are visible because the prolonged catheter drainage had reduced the inflammatory reaction in the ducts. The distal segment of the common duct did not visualize because the sphincter of Oddi had relaxed and the lipiodine, as in the duodenum.

Fig. 5. Case 6. Showing the marked reduction in the size of the biliary duct following 23 days of continuous drainage.

fluids entered the duodenum. (Without encountering any hindrance, therefore proving the common duct to be patent. Because of the chronic stasis of bile and the acute infection of the biliary tract, both the gall bladder and the common duct were drained.)

Seven days following the operation, 4 cubic centimeters of lipiodine (Ciba) was introduced into the gall bladder through the cholecystostomy tube. The oil escaped around the drainage tube and only a very small amount entered the common duct, which confirmed the operative findings of an inflammatory occlusion of the cystic duct (Fig. 4). Six days later a second roentgenogram was made following the instillation of 60 cubic centimeters of lipiodine. The gall bladder was easily filled and the oil immediately passed into the choledochus because the cystic duct was now open. During the introduction of the radiopaque oil, the patient complained of severe epigastric pain similar to her previous colic-like attacks. Evidently the common duct was being distended but what was preventing the oil from entering the duodenum? Roentgenograms taken immediately after the injection of the oil indicated that there was mechanical blockade of the intraluminal orifices of the common duct causing a retention of the lipiodine (Fig. 5). X-ray films taken 3 minutes later disclosed that this temporary obstructing mechanism had completely disappeared for the lipiodine was seen to be in the duodenum and upper jejunum.

This study presents roentgenographic evidence of the futility of attempting immediate drainage of the entire biliary tract by performing a cholecystostomy in cases of acute

cholecystitis and cholangitis in which the inflammatory edema has occluded the cystic duct. If such patients are so unfortunate as to have a concomitant spasticity of the common duct sphincter with bile stasis, then the drainage of the gall bladder merely relieves the pressure on that organ without mitigating the stasis within the ductal system. It was interesting to note that the patient complained of the typical pains of biliary colic during the interval when the spastic sphincter caused a retention of the lipiodine and that the pains did not subside until the sphincter relaxed and permitted the oil to enter the duodenum. This again demonstrates that a hypertonicity of the sphincteric mechanism of the common duct can occur in the presence of an acute infection.

CASE 4. Mrs. A. C. housewife, aged 5 years, entered the hospital complaining of "gall trouble." She had suffered from paroxysms of nausea and vomiting associated with epigastric distress for the last year and a half. During the past 9 months she had been persistently jaundiced, her stools had been acholic, and she had lost 65 pounds of weight.

Examination showed a malnourished, asthenic, deeply jaundiced woman. The liver extended 4 inches below the costal margin. The gall bladder could not be palpated nor did it concentrate the cholecystographic dye. The van den Bergh test was strongly positive in both the direct and indirect



cystic duct and gall bladder indicate a chronic inflammatory reaction. The extrahepatic bile ducts were not dilated but the infection had produced a fibrosis and induration of their walls. In spite of the long standing infection of the biliary ductal system, however, the choledochal sphincter functioned normally, permitting the lipiodine to enter the duodenum immediately. Thus, it would seem that infection *per se* does not always initiate a functional derangement of the sphincteric mechanism of the ampulla. It also demonstrates that a chronic infection of the hepatic system does not cause a dilatation of the bile ducts unless there is a co-existing obstruction, such as stones, strictures, kinks, tumors, or sphincterismus.

CASE 6 C M, aged 69 years, had had "stomach trouble" for 35 years, characterized by bloating, belching of gas, indigestion, and passage of flatus. Over a period of 8 years he had suffered from recurrent attacks of jaundice, at which times his stools were acholic and his urine acquired a very dark color. He had lost 55 pounds of weight during the past 10 months.

Examination disclosed the skin to be deeply jaundiced. There was a large, firmly fixed mass in the epigastric area. The liver, spleen, gall bladder, and kidneys were not palpable. Cholecystograms revealed a non-functioning gall bladder with several calculi apparently in the common duct. During his pre operative period he had several chills with a febrile reaction of 106 degrees F, which suggested a cholangitis secondary to an intermittent calculous obstruction. The large tumor mass, the rapid loss of weight, and the persistent jaundice made the diagnosis of pancreatic malignancy associated with cholelithiasis seem very plausible.

A laparotomy exposed a dark green, nutmeg liver, somewhat enlarged, with a firm, tense fibrotic capsule. The gall bladder was about twice normal size, and its walls were very thick, indurated, and edematous. The cystic duct was patent. The common duct was about three times greater than normal. After aspirating 60 cubic centimeters of black viscid bile, several small stones could be felt in the hepatic ducts. The pancreas was somewhat enlarged, firm, and indurated, but did not present the stony hardness of a malignancy. A cholecystectomy and choledochostomy were performed after removal of several small stones from the hepatic ducts. Painstaking examination failed to show any gross obstruction at the ampulla of Vater.

Visualization studies were deferred until the twelfth postoperative day, at which time 40 cubic centimeters of lipiodine (Ciba) was injected into the choledochus. Roentgenograms were taken immediately and evidenced a marked dilatation of the

common duct. The hepatic ducts were not outlined because the relaxed sphincter had permitted the oil to escape into the duodenum (Fig 10). These same findings were present on similar radiographic studies made on the twenty-ninth (Fig 11) and thirty-third (Fig 12) postoperative days. They corroborate Whitaker's assertion that the gall bladder and bile ducts do not become filled or distended if the sphincter of Oddi is relaxed.

These observations signify that a chronic biliary stasis, hepatic congestion, dilatation of the bile ducts, the presence of calculi in the ducts, and a generalized infection of the biliary system, with a concomitant pancreatitis, apparently do not always increase the tonicity of the sphincter of Oddi or interfere with its ability to relax.

CASE 7 J H, farmer, 53 years of age, entered the hospital because of a "gaseous indigestion." During the past 4 years he had been annoyed by the passage of flatus, belching of gas, and epigastric distress. Intermittent attacks of sharp colic-like pains in the right subcostal area frequently required morphine for their relief. He denied having been jaundiced.

Just beneath the right costal margin there was a firm, tender, ovoid mass. The liver did not seem to be enlarged. The skin and sclera were definitely jaundiced, the icteric index being 12.

Exploration revealed a moderately distended gall bladder which contained many small calculi. The cystic duct contained no stones. The common duct was twice its regular size and, in its retroduodenal portion, there was a small lobulated mass which was thought to be either an enlarged lymph node or an incarcerated intramural calculus. Upon opening the common duct a well developed annular stricture was found just distal to the junction of the cystic and hepatic ducts, which had diminished the diameter of the choledochus to about one-fourth its original size. Technically it was impossible to excise the stricture and then establish the continuity of the bile ducts, nor could a hepatico-enterostomy be done. A cholecystostomy and choledochostomy were performed as these conservative procedures would permit a cholecysto-enterostomy to be done at a later date should the inflammatory scar tissue occlude the common duct. Careful examination disclosed that the intestinal portion of the common duct was patent, therefore, the fibrous band was divided and a "T" tube inserted in such a manner that one limb of the "T" dilated the constricted portion of the duct.

Two days after operation 40 cubic centimeters of lipiodine (Ciba) was introduced into the gall bladder through the drainage tube. Roentgenograms were taken immediately following the injection and again in 20 minutes. In both instances the gall bladder was clearly outlined but the radiopaque media had been unable to traverse the occluded



Fig. 5, left: Case 7. On the eighth postoperative day 60 cubic centimeters of liposolium was injected into the choledochostomy tube. The cystic duct was then patent for the oil entered the choledochos and duodenos. This is in contrast to figure 5, right above, the unrelaxed cystic duct.  
Fig. 6: Case 7. Roentgenogram made after bile ducts had been drained for 8 days. Note the marked reduction in their size. The choledochal sphincter is relaxed (Compare with Fig. 14 as both plates were made following injection of common duct.)

cause a retention of bile the stagnant biliary secretions then become infected and favor the formation of calculi? In order to answer these questions the following studies were carried out:

CASE 5. Mrs. L. B. housewife, 43 years of age, had had severe "gall stone attacks" for the past years. The acute exacerbations are frequently associated with nausea, vomiting, and prostration, but no jaundice.



Fig. 7: Case 8. Liposolium was injected into the cystic duct. The bile ducts are not opacified even though the roentgenograms were made immediately after the introduction of the oil. The relaxed choledochal sphincter had permitted the oil to enter the duodenosum.

Physical examination disclosed tenderness in the right hypochondrium but the gall bladder as not palpable. The an den Bergh reaction did not evidence a bile retention and the icteric index as 4.5. Radiological studies depicted non functioning gall bladder filled with small calculi.

At operation the liver as found to extend 16 inches below the right costal margin. Its capsule as thickened and scarred, particularly in the region of the gall-bladder fossa. The walls of the gall bladder were inflamed, hyperemic, and edematous. Dense adhesions held it in firm position to the duodenum. The inflammation and edema had obliterated the lumen of the cystic duct. The choledochos appeared normal except for slight fibrosis of its walls, there being no evidence of stone stricture, dilatation or neoplasia. In fact, there was nothing to arouse suspicion or to warrant drainage of the common duct. The gall bladder was removed and for therapeutic as well as in estigative reasons.

A catheter as inserted through the stump of the cystic duct to drain the common hepatic radicals.

On the eighth postoperative day 4 cubic centimeters of liposolium (Ciba) as injected into the drainage tube. Roentgenograms made immediately after this injection failed to show any evidence of bile stasis or dilatation of the bile ducts. In fact, the major portion of the oil had already entered the jejunum, indicating relaxed choledochal sphincter (Fig. 9).

This case represents a generalized infection of the entire biliary tree. The diffuse scarring, fibrosis, and lymphocytic infiltration of the

dochus, it may still respond to the proper physiological and pharmacological stimuli. While studying the effects of secretin-cholecystokinin injections on the duodenal secretions of normal subjects, Ivy and his collaborators made some interesting observations. In one instance, they passed the duodenal tube, and at first recovered normal bile, but all at once the flow of bile stopped. This they attributed to a spasm of the choledochal sphincter. Then a solution of secretin-cholecystokinin was injected. A copious flow of pancreatic juice resulted which was not bile stained. Ten minutes later, the patient complained of distress in the right subcostal area. Within 50 minutes, the pain was so severe that relief was sought. Magnesium sulphate was then introduced into the duodenum and a sudden gush of bile evidenced a relaxation of the common duct sphincter. The pain disappeared with the diminution of the intraductal pressure.

Westphal demonstrated that a spasm of the common duct sphincter is capable of producing biliary colic. He inserted a tube into the duodenum and initiated evacuation of the gall bladder by introducing olive oil. After aspirating several samples of duodenal bile, which signified the sphincter of Oddi was relaxed, he gave a rather large dose of pilocarpine. (In dogs, this drug causes the gall bladder to contract, but prevents the evacuation of the common duct by causing a contraction of the choledochal sphincter.) After administering the pilocarpine, the flow of bile into the duodenum stopped and the patient complained of gall-bladder distress. This pain was not relieved until sufficient atropine was given to overcome the effects of the pilocarpine, at which time bile could again be recovered from the duodenum. Such experiences indicate that the choledochal-sphincteric mechanism can contract with sufficient force to prevent the bile from entering the duodenum and that the resultant increase in intraductal pressure can produce pain.

Biliary dyssynergia offers a plausible explanation for several misunderstood clinical problems.

First, it presents a rational physiological conception of the so called "gall-stone colic of

Krukenberg" and "hepatic neuralgia" in which one finds a distended but normal appearing gall bladder without evidence of gross obstruction. A spastic common duct sphincter interfering with the free egress of bile into the duodenum produces a sufficient back pressure to dilate the bile ducts and gall bladder, thus causing pain and discomfort. The absence of infection would account for the normal appearance of the gall-bladder wall. Such patients are not always relieved by a cholecystectomy as this apparently does not correct the dysfunction of the bile-duct sphincter. Possibly the removal of an appendix which was causing a reflex spasm of the sphincter, or the correction of bowel habits, or dietary regulation, may account for improvement in some cases.

Second, a dyssynergia of the choledochal-sphincteric mechanism presents a rational concept for the occurrence of cholangitis and inflammation of the biliary tree, particularly those varieties not preceded by stones or strictures. The hypertonic sphincter favors a retention of the biliary secretions, the stagnant bile then becomes infected, and the infection disturbs the secretory and absorptive functions of the gall bladder and ducts as well as upsetting the delicately poised chemical equilibrium of the bile components, thus initiating the formation of calculi. In such cases the removal of the diseased gall bladder may not be entirely curative, for it does not necessarily change the intrinsic motor derangement of the common duct sphincter.

Strauss operated on 22 patients having a generalized infection and dilatation of the extrahepatic biliary system in which he was unable to demonstrate any obstructive agent. He felt that the bile stasis was secondary to an inflammatory duodenitis thus confirming the observations of Crain and Walsh that an experimentally induced duodenitis interferes with evacuation of the gall bladder. While it is possible that an inflammatory swelling of the duodenal wall could occlude the common duct, such instances must be extremely rare for in 7 patients having a generalized infection of the biliary tract, we failed to find any evidence of obstructing duodenitis. In 5 instances, the common duct sphincter was com-

cystic duct (Fig. 13). This again shows that cholecystostomy does not allow decompression of liver and biliary ducts. Lipiodol was then injected into the "T" tube, thus outlining the dilated common duct. The released splanchnic of Oddi permitted the major portion of the oil to escape into the duodenum (Fig. 14).

Sixteen days later 60 cubic centimeters of lipiodol was injected into the gall bladder and much to our surprise we found the cystic duct to be patent (Fig. 5). This demonstrated the value of prolonged drainage in cases of biliary stasis, for decompression of the gall bladder and common bile duct had permitted the inflammatory edema of the cystic duct and biliary radicals to subside (Fig. 10). The hepatic ducts and the proximal three-fourths of the common duct were of normal size and contour but the distal one-fourth, the portion beyond the lower limb of the "T" tube, could not be visualized. Was there an obstruction in the lower end of the "T" tube which prevented the oil from entering the ampulla of Vater? Apparently not, for the lipiodol was seen in the upper jejunum. The released splanchnic of Oddi had permitted the lower segment of the common duct to evacuate its oily content into the intestinal lumen.

Here was confirmatory evidence that gall stones, cholecystitis, inflammation, strictures, fibrosis of the walls of the bile ducts, and even the presence of a foreign body such as the "T" tube, do not necessarily interfere with normal relaxation or function of the choledochal sphincter.

**CASE 8.** Mrs. A. A. housewife, 39 years of age, had had gall-bladder colic since her first pregnancy two and one half years ago. Frequent exacerbations followed the initial attack, associated with nausea, vomiting, jaundice, and acholic stools. Physical examination and laboratory studies were normal with the exception of two cholecystograms which demonstrated a poorly functioning, dilated gall bladder containing several stones.

When the abdomen was entered, the gall bladder was found to contain three stones, and it was distended by yellow brown bile. The walls of the cystic duct were indurated, edematous, and fibrosed. The common and hepatic bile ducts were normal, but the head of the pancreas was somewhat enlarged and indurated. After performing cholecystectomy a No. 3 catheter was inserted into the ampulla of the cystic duct for postural visualization studies.

Forty cubic centimeters of lipiodol was introduced into the common duct. The bile ducts were not visualized because the oil immediately entered the duodenal tract. An additional 4 cubic centimeters of lipiodol was injected through the drainage tube but it flowed unimpeded into the intestinal lumen, hence, the sphincter of the common duct was relaxed (Fig. 7).

**CASE 9.** Mrs. A. A. housewife, 43 years of age, entered the hospital with the diagnosis of gall stones. During the past 9 months she had had several attacks of biliary colic. Examination and laboratory studies failed to show any abnormalities except a non-functioning gall bladder.

At operation the liver was found to be of normal size. Its capsule was accented, thickened, and fibrosed. The gall bladder was moderately distended and its walls were thick, indurated, and impregnated with fat. Two large stones were incarcerated in a sacculus at the junction of the gall bladder with the cystic duct. A viscid, bile stained secretion was aspirated from the gall bladder from which luxuriant cultures of *Bacillus coli* and gram negative bacilli were obtained. The common and hepatic ducts were not dilated, nor could stones be palpated there. The ampulla appeared normal. A cholecystectomy was performed and a No. 30 catheter sutured into the cystic duct for functional studies.

Forty-eight hours later 40 cubic centimeters of lipiodol was injected into the choledochus through the drainage tube. The bile ducts were not visualized for the oil had escaped into the duodenum. This roentgenogram is similar to that in Case 8 and is therefore not presented.

#### ANALYSIS OF STUDIES

Analysis of these studies indicates that some individuals may have a dysfunction of the choledochal sphincter resulting in a chronic retention of bile while others may have a normally functioning sphincteric mechanism even in the presence of infection, stones, strictures, kinks, and associated pancreatitis. Such a concept is compatible with the observation that all sphincters of the body may at some time or other deviate from the normal by being too tight or too loose. A spasm of the sphincteric mechanism of the cardiac end of the stomach results in the stasis of food in the esophagus followed by regurgitation. In spite of the increased peristaltic action which attempts to overcome the physiological obstruction. A hypertonicity of the pyloric sphincter often initiates retention of gastric content. A spasticity of the anal sphincters may cause constipation and the hypertonic contraction of the vesical sphincter often interferes with the complete emptying of the urinary bladder. Then why should we not expect a dysynergia of the choledochal sphincter?

Even though the spastic bile duct sphincter produces an anatomic blockade of the choledochus,

the demonstration of a relaxed sphincter in 5 cases would seem to negate such a criticism. Oils, particularly olive oil, are active cholagogues, therefore, they should expedite the evacuation of the biliary tract rather than favor a stasis.

#### SUMMARY

1 Clinical and experimental investigations indicate that a hypertonicity or dyssynergia of the choledochal sphincter may mechanically interfere with the evacuation of the gall bladder and bile ducts, thus producing a stasis of bile with a dilatation of the biliary radicals. Such a sphincterismus was demonstrated in 4 patients by direct roentgenographic visualization of the bile ducts following the introduction of lipiodine. In one instance spastic contraction of the common duct sphincter persisted for 3 hours before it relaxed and permitted the lipiodine to enter the duodenum.

2 The dyssynergia of the common duct sphincter may be independent of, or associated with, a generalized infection of the biliary tract, the presence of stones, strictures, kinks, or pancreatitis. The extirpation of the gall bladder, the removal of the stones, the division of the stricture, and the drainage of the infected bile ducts do not always overcome the spasticity of the sphincter, for, in some cases, it persisted after these operative measures.

3 Physiological evidence indicates that the choledochal-duodenal-sphincteric mechanism has sufficient contractile force to prevent the flow of bile into the duodenum, thereby increasing the intraductal pressure and causing pain and discomfort. Such a concept offers a rational explanation for occurrence of "gall-stone colic" in the absence of stones or infection, and for the so called "hepatic neuralgia" and accounts for the persistence of gall-bladder distress in some cholecystectomized patients.

4 A dyssynergia, or spastic dysfunction of the choledochal sphincter, provides an anatomical blockade of the common duct, resulting in a retention of bile. The stagnant bile becomes infected, and calculi are then precipitated. In such cases a cholecystectomy would not necessarily be curative, for following the removal of the gall bladder, the in-

trinsic spasm of the common bile-duct sphincter may continue. Four patients having a spasticity of this sphincter were studied by lipiodine visualization for as long as 33 days following a cholecystectomy, and the sphincterismus still persisted.

5 It is very probable that the proper post-operative medical regimen, including those substances which relax the choledochal sphincter such as atropine, magnesium sulphate, or fats, would do much to correct the abnormal spasticity of the choledochal sphincter and thus tend to minimize the unsatisfactory results which sometimes follow cholecystectomies.

#### BIBLIOGRAPHY

- 1 ASCHOFF, L., and BACMEISTER, A. Die Cholelithiasis. Jena. G. Fischer, 1909.
- 2 BERG, J. Studien ueber die Funktion der Gallenwege unter normalen und gewissen abnormen Verhaeltnissen. Acta chirurg. Scand., 1922, Suppl. 2, 1-185.
- 3 BOYDEN, E. A. Analysis of reaction of human gall bladder to food. Anat. Rec., 1928, 40, 147-189.
- 4 BURGET, G. E. Regulation of flow of bile: effect of eliminating sphincter of Oddi. Am. J. Physiol., 1926, 81, 422-430.
- 5 CRAIN, R. C., and WALSH, E. L. Effects of acute chemical duodenitis upon emptying time of the gall bladder, experimental study. Surg., Gynec. & Obst., 1931, 53, 753-759.
- 6 ELMAN, R., and MCMASTER, P. D. The physiological variations in resistance to bile flow in the intestines. J. Exper. Med., 1926, 44, 151.
- 7 GIORDANO, A. S., and MANN, F. C. Sphincter of choledochus. Arch. Path., 1927, 4, 943-957.
- 8 IVY, A. C. Physiology of the gall bladder. Physiol. Rev., 1934, 14, 1-102.
- 9 IVY, A. C., and SANDBLOM, P. Biliary dyskinesia. Ann. Int. Med., 1934, 8, 115-122.
- 10 JUDD, E. S., and MANN, F. C. The effects of removal of the gall bladder. Surg., Gynec. & Obst., 1917, 24, 437.
- 11 KRUKENBERG, H. Ueber Gallenblasenkoliken ohne Gallensteine. Klin. Wchnschr., 1903, 40, 660.
- 12 LUETHI, H. C. Studies on flow of bile into duodenum and existence of sphincter of Oddi. Am. J. Physiol., 1931, 99, 237-252.
- 13 MELTZER, S. J. Diseases of the bile-ducts and gall bladder. Am. J. M. Sc., 1917, 153, 469.
- 14 NEWMAN, C. Physiology of the gall bladder and its functional abnormalities. Lancet, 1933, 1, 785-841, 896.
- 15 NUBER, J. F. Studien ueber das extrahepatische Gallenwegssystem. Frankfurt. Ztschr. f. Path., 1931, 41, 454-511.
- 16 ODDI, R. D'une disposition a' sphincter speciale de l'ouverture du canal choledoque. Arch. ital. de biol., 1887, 8, 317-322.
- 17 Idem. Sull' tonicita dello sfintere del coledoco. Arch. per le sc. med., 1888, 12, 333-339.
- 18 PUESTOW, C. B. The discharge of bile into the duodenum. Arch. Surg., 1931, 23, 1013-1029.

pletely relaxed and the lipiodine passed unimpeded into the intestinal canal. In the 4 patients having an apparent obstruction at the duodenal end of the common duct no evidence of a duodenitis was found. The ducts were patent and the blockade was evanescent. An inflammatory obstacle should not disappear in 10 minutes or 35 minutes after the introduction of the oil. Lipiodine visualization of the common bile duct, supplemented by direct operative examination indicates that bile retention is caused by a spasticity of the sphincter of Oddi and not by a duodenitis.

Third, a dyssynergia of the choledochal sphincter could be responsible for the persistent gall-bladder distress which is occasionally not relieved by a cholecystectomy. The spastic dysfunctioning sphincter inhibits the free escape of the liver bile into the duodenum causing an accumulation of bile and increasing the intraductal pressure until the extrahepatic radicals become dilated. Judd and Mann have demonstrated that the dilated bile ducts may contain more bile than a normal gall bladder. The dilatation usually continues until the sphincter itself becomes dilated or is unable to withstand the increased pressure. If the sphincter of Oddi is destroyed no such dilatation occurs. Following removal of the gall bladder Puestow noted that the bile did not emerge into the duodenum by spurts as it does normally but that there was a constant dribble, indicating an overflow retention. Repeated lipiodine visualization studies were made on 4 cholecystectomized patients for as long as 33 days after their operations, and each of them exhibited a contracted hypertonic sphincter which was producing a physiological block of the common duct. In one instance the sphincterismus had produced such an increased intraductal pressure that the stump of the cystic duct became dilated, forming a diverticulum. These dilatations were not due to a neurogenic atonia of the bile ducts attributed to the operative intervention, because roentgenographic studies evidenced an increased tone—even a hyperspasticity of the sphincter. Five other cholecystectomized individuals had an atonic, relaxed sphincter when similarly examined. Apparently then this sphincteric mechanism does not always

become paralyzed following the extirpation of the gall bladder but in some cases its persistent spasm may continue to produce a physiological block resulting in pain and distress.

Relief of these persistent symptoms depends on obtaining a relaxation of this spastic sphincter. Westphal has demonstrated that it is innervated by the autonomic nervous system and hence the hypertonicity can be relieved by atropine. Meltzer, Lyons, and Ivy agree that the intraduodenal instillation of magnesium sulphate immediately relaxes the choledochal sphincter and permits the evacuation of the bile ducts. Newman accomplishes the same end by using olive oil. Such operative measures as a choledochal enterostomy or a longitudinal division of the sphincter of Oddi could possibly be employed to overcome this increased intraductal pressure; however such radical procedures should not be advocated until we have a more accurate physiological concept of biliary dyssynergia. It seems that medical regimen will do much to minimize the discomfort caused by a spasticity of the choledochal sphincter.

#### TECHNIQUE

A uniform technique was followed throughout these studies. Two parts of lipiodine (Ciba) and one part of olive oil were heated to body temperature and the resulting mixture was permitted to flow into the drainage tube by gravity. Positive pressure was used in only those cases having a spastic contraction of the choledochal sphincter. In such instances the patients complained of hepatic distress before sufficient pressure could be used to overcome the hypertonic sphincter. It was found that if the patient was placed in the Trendelenburg position during the introduction of oil the biliary radicals were better visualized. Roentgenograms were taken immediately following the introduction of the oil. If there was a retention of lipiodine in the bile ducts then subsequent roentgenograms were taken at 25 and 35 minute periods. Fluoroscopic studies were made in some cases.

One naturally wonders whether the lipiodine itself might not cause a contraction of the sphincter and a retention of the oil but

the demonstration of a relaxed sphincter in 5 cases would seem to negate such a criticism. Oils, particularly olive oil, are active chologogues, therefore, they should expedite the evacuation of the biliary tract rather than favor a stasis.

#### SUMMARY

1 Clinical and experimental investigations indicate that a hypertonicity or dyssynergia of the choledochal sphincter may mechanically interfere with the evacuation of the gall bladder and bile ducts, thus producing a stasis of bile with a dilatation of the biliary radicals. Such a sphincterismus was demonstrated in 4 patients by direct roentgenographic visualization of the bile ducts following the introduction of lipiodine. In one instance spastic contraction of the common duct sphincter persisted for 3 hours before it relaxed and permitted the lipiodine to enter the duodenum.

2 The dyssynergia of the common duct sphincter may be independent of, or associated with, a generalized infection of the biliary tract, the presence of stones, strictures, kinks, or pancreatitis. The extirpation of the gall bladder, the removal of the stones, the division of the stricture, and the drainage of the infected bile ducts do not always overcome the spasticity of the sphincter, for, in some cases, it persisted after these operative measures.

3 Physiological evidence indicates that the choledochal-duodenal-sphincteric mechanism has sufficient contractile force to prevent the flow of bile into the duodenum, thereby increasing the intraductal pressure and causing pain and discomfort. Such a concept offers a rational explanation for occurrence of "gall-stone colic" in the absence of stones or infection, and for the so called "hepatic neuralgia" and accounts for the persistence of gall-bladder distress in some cholecystectomized patients.

4 A dyssynergia, or spastic dysfunction of the choledochal sphincter, provides an anatomical blockade of the common duct, resulting in a retention of bile. The stagnant bile becomes infected, and calculi are then precipitated. In such cases a cholecystectomy would not necessarily be curative, for following the removal of the gall bladder, the in-

trinsic spasm of the common bile-duct sphincter may continue. Four patients having a spasticity of this sphincter were studied by lipiodine visualization for as long as 33 days following a cholecystectomy, and the sphincterismus still persisted.

5 It is very probable that the proper post-operative medical regimen, including those substances which relax the choledochal sphincter such as atropine, magnesium sulphate, or fats, would do much to correct the abnormal spasticity of the choledochal sphincter and thus tend to minimize the unsatisfactory results which sometimes follow cholecystectomies.

#### BIBLIOGRAPHY

- 1 ASCHOFF, L., and BACHMEISTER, A. *Die Cholelithiasis*. Jena G. Fischer, 1909.
- 2 BERG, J. Studien ueber die Funktion der Gallenwege unter normalen und gewissen abnormen Verhaeltnissen. *Acta chirurg. Scand.*, 1922, Suppl. 2, 1-185.
- 3 BOYDEN, E. A. Analysis of reaction of human gall bladder to food. *Anat. Rec.*, 1928, 40, 147-189.
- 4 BURDET, G. E. Regulation of flow of bile: effect of eliminating sphincter of Oddi. *Am. J. Physiol.*, 1926, 81, 422-430.
- 5 CRAIN, R. C., and WALSH, E. L. Effects of acute chemical duodenitis upon emptying time of the gall bladder, experimental study. *Surg., Gynec. & Obst.*, 1931, 53, 753-759.
- 6 ELMAN, R., and MCMASTER, P. D. The physiological variations in resistance to bile flow in the intestines. *J. Exper. Med.*, 1926, 44, 151.
- 7 GIORDANO, A. S., and MANN, F. C. Sphincter of choledochus. *Arch. Path.*, 1927, 4, 943-957.
- 8 IVEY, A. C. Physiology of the gall bladder. *Physiol. Rev.*, 1934, 14, 1-102.
- 9 IVEY, A. C., and SANDBLOM, P. Biliary dyskinesia. *Ann. Int. Med.*, 1934, 8, 115-122.
- 10 JUDD, E. S., and MANN, F. C. The effects of removal of the gall bladder. *Surg., Gynec. & Obst.*, 1917, 24, 437.
- 11 KRUKENBERG, H. Ueber Gallenblasenkoliken ohne Gallensteine. *Klin. Wchnschr.*, 1903, 40, 660.
- 12 LUETH, H. C. Studies on flow of bile into duodenum and existence of sphincter of Oddi. *Am. J. Physiol.*, 1931, 99, 237-252.
- 13 MELTZER, S. J. Diseases of the bile-ducts and gall bladder. *Am. J. M. Sc.*, 1917, 153, 469.
- 14 NEWMAN, C. Physiology of the gall bladder and its functional abnormalities. *Lancet*, 1933, 1, 785-841, 896.
- 15 NUBOER, J. F. Studien ueber das extrahepatische Gallenwegssystem. *Frankfurt. Ztschr. f. Path.*, 1931, 41, 454-511.
- 16 ONDI, R. D'une disposition a' sphincter speciale de l'ouverture du canal choledoque. *Arch. ital. de biol.*, 1887, 8, 317-322.
- 17 Idem. Sull tonicità dello sfintere del coledoco. *Arch. per le sc. med.*, 1888, 12, 333-339.
- 18 PUESTOW, C. B. The discharge of bile into the duodenum. *Arch. Surg.*, 1931, 23, 1013-1029.

- 9 POTTER, J C and MARY, F C. Pressure changes in the biliary tract. *Am. J. M. Sc.* 1926, 7 202-7
10. SMARINO, P., and KASABACH, H. H. Duodenal stenosis effect of chronic duodenal obstruction on evacuation of the gall bladder. *Arch. Surg.* 1933, 96 684-697
11. SCHÖNLEIN, B. and NIEMEN, H. Die Erkrankungen der steinstreuen extrahepatischen Gallenwege. *Verh. d. deutsch. Gesellsch. f. innere Med.* 1932, 44 102-154
12. SCHÖNLEIN, V. Über die "Stauungsgallenabzesse." *Zentralbl. f. Chir.* 1926, 47 57
13. STRAUSS, A A. STRAUSS, F P. CRAWFORD, R A and STRAUSS, H A. Chronic biliary stasis treated by choledochoduodenostomy and gastro-enterostomy. *J. Am. M. Ass.* 1928, 305 171.
14. WESTPHAL, K. Muskelinfection, Nervensystem und Pathologie der Gallenwege. Untersuchungen über den Schmerzursprung der Gallenwege und seine ausstrahlende Reflexe. *Zschr. f. klin. Med.* 1912, 96 22-30
15. WESTPHAL, K. GLEICHMANN, F and MAYER, W. Gallenweginfektion und Gallensteinleiden. Berlin. Julius Springer 1931.
16. WHITAKER, L R and EMERSON, W C. Emptying gall bladder in pregnancy. *Am. J. Physiol.* 1928, 24 5 6-5 9
17. WHITAKER, R. The mechanism of the gall bladder. *Am. J. Physiol.* 1926, 78 411.
18. Idem. Experiences with cholecystography, including observations on the functions of the gall bladder. *J. Am. M. Ass.* 1926, 86 20-243



## PRACTICAL ROENTGEN PELVIMETRY

## A COMPARISON OF METHODS IN 100 CASES

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EXTERNAL pelvimetry, while valuable, may be fallacious. There are many occasions upon which the obstetrician may be greatly benefited by a more accurate knowledge of the measurements and shape of the female pelvis, and of the relationship between the fetal head and its bony canal. Roentgen pelvimetry is a simple procedure and one may employ it without any fear of damaging the fetus. Whereas it may not be practical or necessary to examine all patients roentgenologically there are certain definite indications. Freiheit states all primiparæ with a diagonal conjugate of 11.5 centimeters or less, or in whom the vertex fails to engage from the thirty-second to the thirty-fourth week, or in whom an unusual presentation occurs, should be subjected to X-ray examination. Multiparæ with histories of previous difficult labors with normally sized infants and multiparæ with a history of fetal death subsequent to operative delivery from below should also be roentgenographed. There are also additional indications for roentgen cephalometry, but we shall confine our attention in this publication to pelvimetry. Recently the value of X-ray examination has also become apparent for women in labor in whom there is some unexplained delay.

Several methods of roentgen pelvimetry have been advanced, and these are chiefly based on either a geometrical or stereoscopic principle. Any line of a given length parallel to a film is to the length of its image produced on the plate as the distance between the target and the line is to the distance between the target and the plate (Fig 1). This is our definition of the geometrical principle. In applying this method to pelvimetry it is necessary to have the pelvic inlet parallel to the plate. This is accomplished by the semi-recumbent position with the upper anterior border of the symphysis pubis and the interspace between the fourth and fifth lumbar

vertebræ at equal distances from the table top. Hypher, Roberts, and Ewer and Bowen report the use of this method. The method described by Thoms eliminates the calculations herein described. He employs the principle that any object placed at a known distance above the film will be magnified in the same degree as any other object placed at the same distance, if the target-film distance is kept constant. The object, if it is a line, need not be parallel to the film to give the same degree of magnification as any other equal line, as long as both lines are identically placed. In practice, Thoms introduces the perforated centimeter grid in the same plane previously occupied by the superior strait. Jarcho reports the use of the centimeter grid also in the lateral view. Jacobs likewise reports on this method for lateral pelvimetry. He employs a separate film, however, for the perforated grid. Using the geometrical principle, Walton has prepared a chart which gives the corrected reading for each distance measured on the film (Fig 2). It is necessary to know the distance from the interspace between the fourth

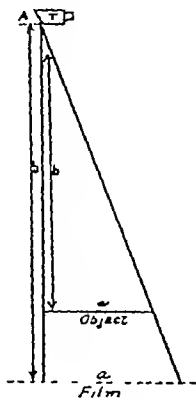


Fig 1 Geometrical principle involved in determining the actual size of an object placed parallel at a distance from the film. Formula  $a' = \frac{a \times b}{b'}$

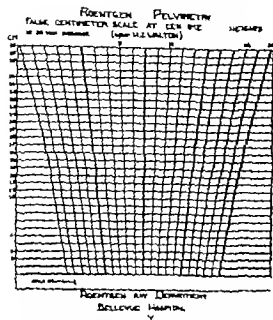


Fig. 2. False centimeter chart (after Walton) used in correcting measurements obtained on roentgenograph and lateral films of pelvis

and fifth vertebra to the plate and to have the inlet parallel to the film to apply this chart. Ball and Marchbanks have designed the pelvcephalometer an instrument which depends on the same principles.

Stereoscopic roentgenometry may be accomplished by reproducing in space the object stereoscoped.

In a method described by Johnson this is done by superimposition of films on a horizontal view box. Wires are attached to a point above the view box corresponding to the position originally occupied by the target and the loose ends are placed on the anatomical landmarks of the film between which the measurements are to be made. The divergence of the wires represents the rays. The position formerly occupied by the object being measured is actually reproduced and measured.

Moloy has devised a stereoscopic viewing box equipped with prisms instead of mirrors which projects the image in space. By his method measurements are made of this image while it is being viewed through the prisms. The image is a true optical reproduction of the subject under stereoscopic vision.

#### COMPARISON OF METHODS

Each method of pelvimetry has certain advantages and certain disadvantages. Stereoscopic technique is superior in its ability to enable one to visualize the relationship between the fetal head and the bony canal. This method also has the added advantage of simplicity in taking the films. The patient may be placed supine, although we have found that better results obtain when the natural lumbar lordosis is increased by placing a sandbag beneath the lumbar vertebrae. The outlet as well as the inlet may be investigated on the stereoscopic plates. However such methods require additional equipment, often quite expensive. The reading and measuring of the plates in the Moloy stereoscope require constant practice. In the hand of one accustomed to this apparatus very accurate measurements are obtained. However we have found that the occasional user will have difficulty in obtaining identical readings each time he measures a given pelvis. It must be emphasized though that only stereoscopic methods give the three dimensional sense and, hence, are superior in establishing fetal head canal relations.

Lateral pelvimetry has certain definite advantages. The anteroposterior diameter of the superior strait is usually measurable. The promontory of the sacrum is easily and accurately located. The fetal head is clearly visualized. This view is especially important in demonstrating the curve of the sacrum and the width and shape of the sacrocaudal notch. Jacobs calls attention to the value of determining the inclination of the inlet to the spinal column. As the angle approaches a perpendicular engagement is facilitated as it approaches a parallel, engagement becomes more difficult. In taking a lateral view the legs must be extended to obtain this information. From the technical standpoint lateral views are easy to obtain and require no additional equipment. Lateral pelvimetry alone nevertheless, has one great shortcoming—it does not reveal the shape of the inlet. The transverse or oblique diameters cannot be measured.

The anteroposterior methods of pelvimetry are the ones most in vogue. The semircumbent position is used and this may easily be

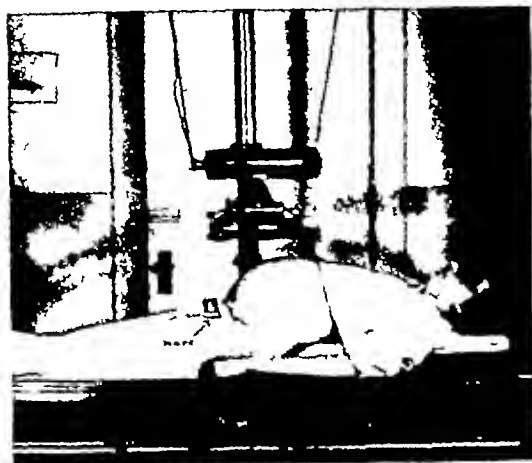


Fig 3. Patient in position for roentgenography of pelvis for the Moloy stereoscopic study. Note the 9 centimeter markers placed just below the symphysis pubis.

accomplished on a Potter-Bucky diaphragm table with some form of support for the hands and feet. According to the method of anteroposterior pelvimetry selected, certain special, though usually inexpensive equipment is necessary. In the Thoms' method the tube stand must be equipped with plumb lines and a grid must be used for the second exposure. Calipers facilitate the use of this technique. It is not necessary to have the conjugata vera exactly parallel to the cassette if the perforated grid is employed although the closer the inlet approaches the parallel the better is the demonstration of the shape of the inlet. In the geometrical anteroposterior method and in methods described by Walton with a calculated chart and by Ball and Marchbanks with their instrument and its calculated disc-chart, the plane of the superior straight must be parallel to the film. All these methods do demonstrate the shape of the inlet although at times it is not possible to state definitely exactly what point represents the promontory of the sacrum. The outlet is not accurately measurable by this method although the bischial spinous diameter is obtainable and it may be considered to be about 3 centimeters above the table top.

#### TECHNIQUE

In carrying out this study we have used two methods that of Moloy with the Moloy



Fig 4. Roentgenograph obtained (one of stereo set) with patient in position shown in Figure 3. The magnified 9 centimeter distance across markers is shown, which is corrected in the precision stereoscope.

stereoscope and that of Walton with his chart. In employing Walton's method we have added the lateral view so that we have had an additional check on the conjugata vera measurement.

The stereoscopic films for the Moloy method are obtained with the patient in a recumbent position (Fig 3). A sandbag is placed under the lumbar spine to alter the pelvic inclination with the plate slightly and thus to facilitate the stereoscopic mensuration. A cardboard strip with two metal markers exactly 9 centimeters apart is placed on the patient just below the symphysis pubis so that the center of the cardboard strip is about at the symphysis and the ends with the metal strips are between the symphysis and the trochanters. The tube is focused over the center of a line joining the anterior superior spines. Target-film distance is 25 inches, stereoscopic shift is 6 centimeters, milliamperes 30, kilovolt peak, 65, seconds, 12-15. These films are viewed in the Moloy stereoscope although the one employed here does not have the armatures described by him (8). Instead, the prisms are moved back and forth until the 9 centimeter distance between the lead strips on the



Fig. 5. Patient in position for roentgenography of the pelvic inlet. Measurements adduced here are corrected according to chart in Figure 6.

cardboard marker coincides with 9 centimeters on a ruler held on the opposite side of the prism from the eyes of the observer. Measurements are then made directly on the optical image in space with the ruler. This eliminates the use of a dried pelvis and accomplishes the same thing (Fig. 4).

The anteroposterior view for the Walton method is obtained by placing the patient in a semirecumbent position (Fig. 5). She rests her hands behind her on the side of the table. We have not found any foot support to be necessary although the sandbags may be used here if desired. The interspace between the fourth and fifth vertebrae is marked and its distance from the table measured. The distance from the upper anterior border of the symphysis pubis to the table is also measured. The patient is instructed to arch her back or change her angle of inclination until the two are equal. Then the anteroposterior diameter of the superior strait is parallel to the film (Fig. 6). Exposures are made with the target film distance 30 inches milliamperes, 30 kilovolt peak, 72 seconds, 15-20. On the film the distance between the promontory of the sacrum and the posterior border of the symphysis pubis about 1 centimeter below the superior border is measured. This is the magnified conjugata vera. The transverse diameter is measured between the widest points

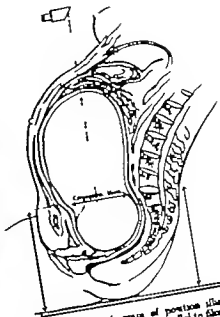


Fig. 6. Schematic diagram of position illustrated in Figure 5 and showing pelvis inlet parallel to film. The distances from the symphysis pubis and fourth lumbar interspace to film are also shown and should be of equal space.

The oblique diameters are measured between the sacro-iliac synchondroses and the opposite iliopectineal eminences and finally the interspinous diameter is measured (Fig. 7). These measurements are then corrected on the Walton chart. For the correction of the anteroposterior diameter of the superior strait the distance from the interspace between the fourth and fifth vertebrae to the table is added to table top-film distance. Using this correction the true anteroposterior diameter is directly measured off on the Walton chart. In applying this method to the transverse diameter we have subtracted 2 centimeters from the distance measured between the interspace between the fourth and fifth lumbar vertebrae and the table as the transverse diameter of the superior strait is about that distance below the anteroposterior diameter. This was first called to our attention by the publication of Ewer and Bowen and subsequent investigation on dried pelvis confirmed the value of such a procedure. For similar reasons we subtract 1 centimeter from the distance between the interspace and table in ob-



Fig 7 Roentgenograph obtained with patient in position shown in Figures 5 and 6. The magnified anteroposterior and transverse diameters are shown. These are corrected according to the geometrical principle. For expediency the chart of Figure 2 is employed.

taining the oblique diameters, although as Ewer and Bowen point out, the anterior end of the oblique line at the pubic spine is higher than the posterior end at the sacro-iliac synchondrosis. The distance of the ischial spine from the table top is not measured, but we have considered the buschial diameter to be 3 centimeters from the table top. This is not accurate and indeed in the buschial diameter the stereoscopic anteroposterior film measurements do not check as closely as they do with the other diameters.

The lateral view of the pelvis is obtained by placing the patient on her side with one trochanter directly over the other with her legs extended (Fig 8). The distance from the midpoint of the interspace between the fourth and fifth lumbar vertebrae to the table is measured. To have a true lateral, the distance between the center of the symphysis pubis and the table should equal this other measurement. The tube is centered over the midpoint of a line connecting the interspace and the symphysis pubis at 30 inches from the plate, milliamperes 30, kilovolt peak, 72, seconds 12. The distance between the sacral promontory and the posterior superior border of the

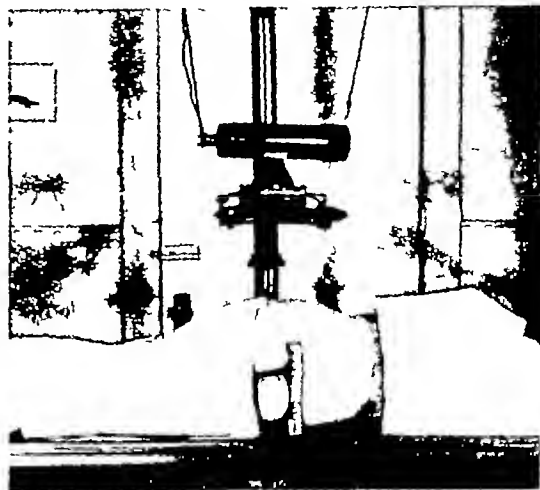


Fig 8 Patient in position for lateral pelvimetry. The distance from the spinous process of the fourth lumbar and the symphysis pubis to the film must be equal to insure parallelism of the conjugata vera and film.

symphysis pubis is measured and corrected on Walton's chart.

#### COMPARATIVE DATA

One hundred women were examined roentgenologically in the X-ray Department of

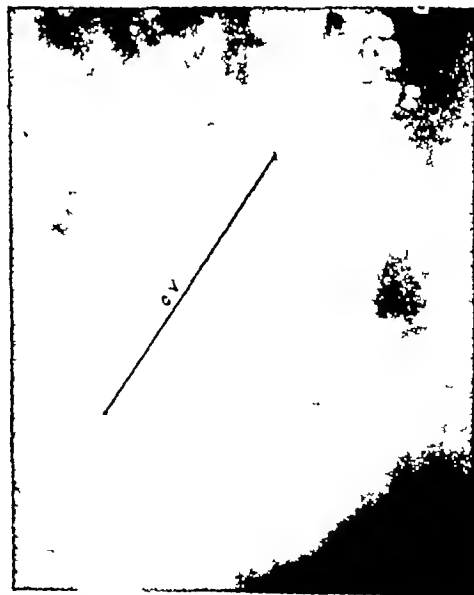


Fig 9 Film obtained with patient in position shown in Figure 8. The magnified conjugata vera is shown; this is corrected as explained in Figure 7.

# SURGERY GYNECOLOGY AND OBSTETRICS

## TABLE L—COMPARATIVE MEASUREMENTS OF EACH CASE

Case	Anteroposterior diameter—Walton	Conjugata vera—Moloy	Transverse diameter—Walton	Transverse diameter—Moloy
1	7	5	6	5
2	7	6	3	3
3	7	9	3	3
4	7	9	3	3
5	7	9	3	3
6	7	9	3	3
7	7	9	3	3
8	7	9	3	3
9	7	9	3	3
10	7	9	3	3
11	7	9	3	3
12	7	9	3	3
13	7	9	3	3
14	7	9	3	3
15	7	9	3	3
16	7	9	3	3
17	7	9	3	3
18	7	9	3	3
19	7	9	3	3
20	7	9	3	3
21	7	9	3	3
22	7	9	3	3
23	7	9	3	3
24	7	9	3	3
25	7	9	3	3
26	7	9	3	3
27	7	9	3	3
28	7	9	3	3
29	7	9	3	3
30	7	9	3	3
31	7	9	3	3
32	7	9	3	3
33	7	9	3	3
34	7	9	3	3
35	7	9	3	3
36	7	9	3	3
37	7	9	3	3
38	7	9	3	3
39	7	9	3	3
40	7	9	3	3
41	7	9	3	3
42	7	9	3	3
43	7	9	3	3
44	7	9	3	3
45	7	9	3	3
46	7	9	3	3
47	7	9	3	3
48	7	9	3	3
49	7	9	3	3
50	7	9	3	3
51	7	9	3	3
52	7	9	3	3
53	7	9	3	3
54	7	9	3	3
55	7	9	3	3
56	7	9	3	3
57	7	9	3	3
58	7	9	3	3
59	7	9	3	3
60	7	9	3	3
61	7	9	3	3
62	7	9	3	3
63	7	9	3	3
64	7	9	3	3
65	7	9	3	3

## TABLE L—COMPARATIVE MEASUREMENTS OF EACH CASE—Continued

Case	Anteroposterior diameter—Walton	Conjugata vera—Moloy	Transverse diameter—Walton	Transverse diameter—Moloy
66	7	9	3	3
67	7	9	3	3
68	7	9	3	3
69	7	9	3	3
70	7	9	3	3
71	7	9	3	3
72	7	9	3	3
73	7	9	3	3
74	7	9	3	3
75	7	9	3	3
76	7	9	3	3
77	7	9	3	3
78	7	9	3	3
79	7	9	3	3
80	7	9	3	3
81	7	9	3	3
82	7	9	3	3
83	7	9	3	3
84	7	9	3	3
85	7	9	3	3
86	7	9	3	3
87	7	9	3	3
88	7	9	3	3
89	7	9	3	3
90	7	9	3	3
91	7	9	3	3
92	7	9	3	3
93	7	9	3	3
94	7	9	3	3
95	7	9	3	3
96	7	9	3	3
97	7	9	3	3
98	7	9	3	3
99	7	9	3	3
100	7	9	3	3

Bellevue Hospital between August 1934 and April 1935. The first 43 cases were examined by the Moloy stereoscopic and Walton antero-posterior methods. The last 57 cases were examined also in the lateral position with the Walton chart for measurements. In Table I the measurements obtained in each case for the conjugata vera and transverse diameter of the superior strait are tabulated. Table II summarizes the discrepancies in measurements between the methods. It is seen that 73 per cent of the cases show no more than 0.5 centimeter difference in the transverse diameter measurement. The differences cited in the tables may be due to variation either way—the Moloy method occasionally reading more and occasionally less than the Walton method. Twenty per cent of cases showed a difference in reading of 0.5 centimeter in the transverse diameter. In the measurement of the conjugata vera, the Walton antero-

TABLE II—SUMMARY OF AMOUNT OF VARIATION IN READINGS OF ANTEROPOSTERIOR AND TRANSVERSE DIAMETERS FOR EACH OF THE METHODS USED

Diameter being measured	Conjugata vera									Transverse diameter		
Methods being compared	Anteroposterior (Walton) Moloy stereoscopic			Anteroposterior (Walton) Lateral (Walton)			Moloy stereoscopic Lateral (Walton)			Moloy stereoscopic anteroposterior (Walton)		
Differences in centimeters	No of cases	Total cases	Per cent	No of cases	Total cases	Per cent	No of cases	Total cases	Per cent	No of cases	Total cases	Per cent
0	12	75	75	13	53	93	7	40	70	16	73	73
1	17			19			7			13		
2	15			8			10			16		
3	12			6			6			9		
4	11			6			4			10		
5	8			1			6			9		
6	6	18	18	2	3	5	2	15	26	8	20	20
7	1			1			1			4		
8	6			0			3			3		
9	4			0			5			4		
10	1			0			4			1		
Over 1 cm	7		7	1		2	2		4	7		7

posterior and Moloy stereoscopic methods checked within 0.5 centimeter in 75 per cent of the cases and between 0.6 and 1 centimeter in 18 per cent of the cases. The lateral pelvic mensuration checked with the Walton anteroposterior method for a difference of 0.5 centimeter or less in 93 per cent of the cases. In only 1 case did these two methods show a variation greater than 0.7 centimeter. The lateral plate measurements compared to the Moloy measurements about as the anteroposterior (Walton) plates did (see Table II). In 7 cases discrepancies were shown of more than 1 centimeter but 5 of these 7 were among the first in which measurements were made. As our technique improved the figures obtained by all methods agreed more closely. The fact that the lateral pelvic measurements of the conjugata vera checked so closely with the anteroposterior film measurements in so many cases indicates only that our technique in carrying out these two methods of geometrical measurement is fairly accurate. However, when these two figures do compare closely and yet are at a considerable variance with the stereoscopic measurement, we are inclined to favor the former as being somewhat more accurate.

#### CONCLUSIONS

In this communication, we have attempted to set forth the principle and technique of the methods we selected for a study of pelvimetry. We may conclude that the methods of anteroposterior pelvimetry and lateral pelvimetry described are simple procedures and give results which agree closely with each other and with those of the stereoscopic method. The reading of the stereoscopic plates according to the method described requires some experience and, of course, the prism stereoscope. There is no reason to believe that the measurements obtained with the stereoscope are more accurate than those obtained by the other methods described. However, this publication deals only with pelvimetry and if the fetal head-bony canal relationship is being investigated the stereoscope is very valuable.

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#### BIBLIOGRAPHY

1. BALL, R. P., and MARCHBANKS, S. S. Roentgen pelvimetry and fetal cephalometry, a new technique. *Radiology*, 1935, 34: 77-84.
2. EWER, J. M., and BOWEN, C. B. Roentgen pelvimetry. *Am J Roentgenol*, 1933, 29: 462-468.

3. FARRAR, J. M. The Thomas method of roentgen pelvimetry and cephalometry. *Radiology* 93, 21 372-380
4. HIRSH, M. The diagnostic value of radiology in obstetric practice. *Brit J Radiol* 93 4 (a) 73
5. JACOBS, J. B. The lateral pelvic roentgenogram. *Am J Obst. & Gynec* 93, 28 27-234
6. JACOBSON, J. Roentgenographic measurements of pelvic and cephalic diameters. *Am J Surg* 93, 4 9-427
7. JOHNSON, C. R. Stereorospectrometry. *Am. J. Surg* 93, 8 5-63
8. MOTOY, H. C. A new method of roentgen pelvimetry. *Am J Roentgenol* 93, 30 714
9. ROWLAND, R. E. Internal pelvimetry by X rays. *Brit J Radiol* 92, 32
10. THOMAS, H. Roentgen pelvimetry. *Radiology* 93 25-130
- WALTON, H. J. Roentgen pelvimetry and cephalometry. *South M J* 93, 1 260-266



## THE ESTROGENIC PRINCIPLE, THE COMMON ETIOLOGICAL FACTOR OF ENDOMETRIAL HYPERPLASIA, UTERINE FIBROIDS AND ENDOMETRIOMAS

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ENDOMETRIAL hyperplasia, uterine fibroids, and endometriomas are three of the very common conditions encountered in the practice of gynecology. All three have been dealt with rather extensively in medical literature, yet only has the etiology of endometrial hyperplasia been generally accepted. The cause of the two tumors is still vague and only general explanations are offered as to their etiology. That these three conditions could possibly have a common etiological background has only recently been entering into medical literature, however, it is the hypothesis of this paper that such is the case, and that the fundamental cause has its origin in excessive stimulation by the ovarian follicular hormone on the endometrium, myometrium and the ectopic locations from which the endometriomas arise. That the action of this hormone is not specific to the uterine endometrium alone, but acts upon the genital tract as a whole, is easily demonstrated (38). When this action on the endometrium is abnormal, causing endometrial hyperplasia, it is equally abnormal in its action upon the myometrium, causing by cellular metaplasia of the uterine muscle cell or cells, the subsequent development of uterine fibroids. Likewise irregularity of action of this hormone on potential serosal cells, by cellular metaplasia of these cells, or by tumor proliferation of aberrant endometrial implants, causes the formation of endometriomas.

### ENDOMETRIAL HYPERPLASIA

The subject of this paper naturally divides itself into 3 parts, and each will be discussed separately. Endometrial hyperplasia is a very common and important gynecological condition. It is characterized by profuse and irregular bleeding from the uterus, hyperplasia of the endometrium of the "Swiss cheese" pattern, excess ovarian follicular hor-

mone in the blood and urine, multiple follicle cysts of the ovary and absence of corpora lutea. From the work of Schroeder and Meyer in Germany, Shaw in England, Graves (14), Fluhman (12), Novak and Martzloff, and Burch in this country, the cause of endometrial hyperplasia has been thoroughly investigated. That the persistent and excessive ovarian follicular hormone stimulation, in the absence of any corpora lutea and with a possible anterior hypophyseal action in the background, is the cause of endometrial hyperplasia has well been established by these observers. In fact, Burch (5) and his co-workers have produced endometrial hyperplasia in spayed animals by the injections of the estrogenic principle. The general acceptance is, at present, that endometrial hyperplasia is the result of the unopposed and continued action of an excess amount of the estrogenic principle derived from the multiple follicle cysts of the ovary.

### UTERINE FIBROIDS

*Histogenesis* What is the cause of uterine fibroids is a question that is asked daily of the gynecologist and one which he can at present answer only in vague generalities. The histogenetic study of fibroids does not reveal in the uterine muscle any certain distinctive myoma mother cells from which might be traced the stages that lead to a proliferating myoma. Robert Meyer (23), Becher, and Heimann have practically settled the question of the histogenesis of uterine fibroids. They have studied in serial sections the smallest myomatous tumors and have found that the earliest appearance of a myoma represents a thickening of the uterine muscle bundles which are directly connected with the normal musculature of the uterus. These tumors are generally devoid of blood vessels and therefore their origin cannot be ascribed to this source, but from the normal uterine muscle itself (15).



Fig. Hyperplasia of the endometrium of the uterus.  
Source.

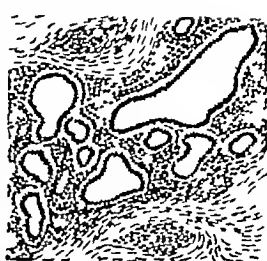


Fig. Endometrial hyperplasia of an ovarian endometrioma. Both slides are taken from the same patient.

On the other hand DeSnoo suggests that the uterus is a very special primitive organ, an organ having a great many undifferentiated cells, *genitoblasts*, which are of very great physiological importance. While these cells in the embryonic life form the uterus proper later on they serve to provide material for the growth of the uterus during pregnancy and for the regeneration of the endometrium during the puerperium. Under pathological conditions these *genitoblasts* can give rise to the formation of uterine fibroids, adenomyomas, and endometriomas. The remarkable thing about these *genitoblasts* is that both under physiological and pathological conditions, their activity and proliferation depend entirely upon the functioning of living ovarian tissue.

It must be admitted, however that the ultimate causation of uterine fibroids is as far from being explained as that of other new growths but the hypothesis here offered is that excessive ovarian follicular hormone stimulation is the igniting factor that causes cellular metaplasia of a certain uterine muscle cell or cells which, if the hormonal stimulation continues, will develop into uterine fibroids.

The exact nature of the action of the estrogenic principle upon uterine tissue is still only partially understood. If hormones are metabolic products of cells, secreted into the blood

stream, it would seem logical to look for action directly upon the cells involved. Opposed to this view is the hormonal stimulation of the vascular control mechanism. There can be little question that this mechanism is involved in some way due to the hyperemic conditions of the organs stimulated (r).

#### ETIOLOGY

Graves (15) has aptly drawn attention that uterine fibroids possess certain attributes that seem to place them in a borderland between physiological hypertrophy and true neoplastic growths. Their great frequency (so per cent of all women over 35) their apparent coincidence with the sexual era, their regression after ablation of the ovarian function, their histological similarity to diffuse hypertrophy and gestation hyperplasia, their structural identity with the normal musculature are all familiar facts that lead to the tumors a physiological glamour which they probably do not deserve.

In determining the ultimate cause of fibroids, it must be considered first whether or not uterine muscle cells possess an inherent growth capacity different from that of smooth muscle in other parts of the body. That such a fact is true is well demonstrated by clinical and histological observations of diffuse uterine

hypertrophy in conditions of "fibrosis uteri" and in gestational hyperplasia. Second, it must be determined whether the uterine muscle is subjected to a specific external stimulus that is able to call forth this growth response. That such a specific stimulus is present is readily shown by the growth action of the estrogenic principle on the myometrium. Clauberg has published roentgenograms demonstrating by means of lipiodol injections the greatly increased size of the cavity of the uterus in a castrated woman after large injections of the follicular hormone. An unlimited number of observers have noted the same effect on animal uteri after the administration of the same hormone. The uterus becomes enormously enlarged because of its rapid growth and increased vascularity—an effect due solely to the hormone elaborated by the graafian follicle (Van Herweden and Corner).

The popular theories of etiology of uterine fibroids are (1) irritation theory—the irritating stimulus of infection stimulates abnormal growth. (2) Circulatory theory—the hyperemic condition of the uterus during pregnancy and the puerperium, when hyperemia is at its peak, rules out this theory. (3) Growth-energy theory—this theory represents an unsatisfied tendency of the uterine muscle to hyperplasia, which finds its natural expression in the enormous growth of pregnancy. When pregnancy does not occur, the uterus manifests an abnormal proliferation in the nature of fibromyomatous growths. (4) Sterility—patients with fibroids exhibit sterility 3 to 4 times as frequently as normal women. Whether sterility is the cause of fibroids or fibroids the cause of sterility is the essential problem. (5) Heredity—occasionally sisters of one family, or mother and daughter will present fibroids, although only 21 women in Lynch's 683 cases gave an indicative family history. (6) Race—fibroids are exhibited about 9 times as frequently in the colored woman as in the white. Such an observation is of interest because of the rarity of this condition in the primitive African savages. The increasing civilization of the Negro woman has inflicted this acquired condition upon her. (36)

Fibroids are comparatively unknown in the lower animals. Sampson suggests such find-

ings are due to lack of true menstruation in these animals, while DeSnoo goes back one step further and ascribes their prevalence in woman to be due to the stronger ovarian activity in humans.

The present tendency is to explain the cause of uterine fibroids on some irregularity of function of the hormones that regulate the growth and physiology of the pelvic organs. However, it must be remembered at the onset that this dysfunction, which is mainly hypophyseal or ovarian, acts as a sexual growth stimulant on the entire genital tract. Not only is endometrial hyperplasia induced by such dysfunction, but the tubal muscularis and mucosa, the myometrium, the vagina, vulva, and breasts are all stimulated to increased mitotic cellular division and hypertrophy. In fact, this estrogenic principle is a growth stimulant to the entire mullerian tract, and the development of abnormal conditions, such as endometrial hyperplasia due to its over action is a manifestation of its dysfunctional act on in only one locality. The myometrium, the tubes, aberrant endometrium, the breasts or any part of the genital tract can likewise express abnormal lesions of growth resulting from its dysfunctional stimulation.

In three former communications (34, 35, 36) the rôle of multiple follicular cysts of the ovary, resulting in hyperestrinism, which stimulates the uterine endometrium to an abnormal hyperplastic condition, was discussed. It was hypothesized that this abnormal estrogenic stimulus affected not only the endometrium, but the myometrium as well. Since fibroids tend to grow slowly, this abnormal estrogenic stimulus would produce immediate hyperplasia of the endometrium and gradually developing fibroids, provided the stimulus was prolonged sufficiently. Such an explanation can easily account for the great prevalence of fibroids in the negro race. The enormous incidence of pelvic inflammatory disease in the negro produces pathological changes in and around the ovaries, resulting in permanent ovarian dysfunction, which will express itself immediately as endometrial hyperplasia, and more latently as fibromyomatous changes in the myometrium.

This hypothesis has been recently supported by King who states "Another fact of interest bearing on the clinical side of endometrial hyperplasia is its frequent association with fibroid tumors. Its frequency would surely exclude its being a chance relationship. It is more commonly found in connection with the smaller tumors, as the large ones, by stretching and pressure are more likely to produce endometrial atrophy. In 114 cases of fibroids, 71 per cent of the cases exhibited hyperplasia of the endometrium. A further suggestive point is found in the frequent combination of endometrial and myometrial hyperplasia."

Allen (2) also lends support to this theory of origin of uterine fibroids. The high incidence of fibromyomas associated with endometrial hyperplasia suggests to Allen the inclusion of these masses of functionless tissue as an end result of hormonal stimulation, another type of cellular metaplasia caused by underlying glandular dysfunction. Such a postulate this author observes, has many interesting and new angles. If accepted as a starting point it will lead into the field of the cause of all benign tumors, while further metaplasia or dedifferentiation carries on directly into the realm of malignancy.

Lewis and Geschickter have shown the presence of the gonadotropic and estrogenic principles in a myoma of the uterus while Zondek and Fluhman (11) have demonstrated a measurable amount of prolactin A in the urine of about one third of their cases of fibroids (Allen, 2).

#### CLINICAL DATA

The present paper is 2 years additional evidence in support of a cause and effect relationship between multiple follicle cysts of the ovary with excess estrogenic hormone secretion immediate production of endometrial hyperplasia and more latent development of uterine fibroids, if the stimulation is sufficiently prolonged.

Forty four cases of endometrial hyperplasia were studied. On each patient a curettage was performed and the curettements diagnosed microscopically as hyperplasia of the endometrium. In no case either by bimanual examination or with the curette, was a uterine

fibroid noted. In addition 20 of the cases (45 per cent) had a laparotomy performed and in no instance was a fibroid found but in every case multiple follicle cysts of the ovaries were observed. After varying intervals, the average being 4 years and 9 months, all 44 patients returned for a second operation because of uterine fibroids, and the findings of the endometrium, myometrium, and ovaries at the time of the second operation are here offered as evidence of an interrelationship between multiple follicle cysts of the ovary endometrial hyperplasia and uterine fibroids.

#### ANALYSIS OF TABLE I

The age limits were well within woman's functional years, 30 to 39 years accounting for 77 per cent of all patients the average being 36 plus years. The symptoms between the first and second operations offer an interesting comparison, the outstanding feature of which was an increase of complaints. Radium caused a temporary amenorrhea in 3 cases, while in 6 cases no benefit was derived from its application. Pregnancy occurred in 2 women after the initial curettage. The average time between the two operations was 4 years and 9 months. The abdomen was opened in 20 patients in addition to the 44 curettages, and in 16 instances of the 20 cases the ovaries were diagnosed either microscopically or operationally as containing multiple follicle cysts. The amount of the curettements was described but since different doctors performed the curettages, the description naturally varies with the operator.

At the second operation the uterus was removed in every instance because of fibroids. Both ovaries were examined in 18 cases, while all the remaining ovarian tissue was removed in 10 a total of 64 per cent. Unless both ovaries or the total ovarian tissue are studied in their entirety it is unwise to draw conclusions concerning the presence or absence of the corpus luteum, since its absence is so importantly related to hyperplasia of the endometrium. In 4 cases developing corpora lutea were found with associated premenstrual endometrium while in 35 cases no ovarian yellow body was observed. Multiple follicle cysts of the ovaries were present in all 44

cases, including those in which the corpora lutea were found. Any explanation for the co-existence of follicle cysts of the ovaries and corpora lutea must be in the nature of an hypothesis. That endometrial hyperplasia is not always a permanent condition is frequently seen just after the puberty age when menstruation disturbed at first, settles down to its normal rhythm. During the transition period between abnormal functional bleeding to normal menstruation, the existence of multiple follicle cysts and corpora lutea might be observed.

The myometrium was hyperplastic in 24 cases, 55 per cent, and was adenomyomatous in 8. Salpingitis and adhesions were noted 38 times, 86 per cent, while ovarian endometrial transplants were present in 22 cases, or 50 per cent. Combining this latter figure with the adenomyomatous findings, endometriomas were found to be present in 28 patients, 64 per cent. Two patients exhibited combined myometrial and ovarian endometriomas. This observation will be discussed subsequently in more detail.

#### DEDUCTIONS

These 44 cases of endometrial hyperplasia, on which a second operation was performed on an average of 4 years and 9 months later for fibromyomatous growths of the uterus, are convincing evidence of a cause and effect relationship of the prolonged and unopposed action of the ovarian follicular hormone on the myometrium and the subsequent development of uterine fibroids. Evidence has been sufficiently advanced for the general acceptance of hyperestrin stimulation of the ovary from multiple follicle cysts as the cause of endometrial hyperplasia. The excess of action of this hormone or its dysfunction is not limited solely to the endometrium, all of the genital tract is stimulated to hypertrophy and hyperplasia by its action. The contention of this paper is that when this hormonal stimulation is of sufficient strength or when its action is unopposed over a lengthy period, it is the igniting factor which causes cellular metaplasia of one or of several of the uterine muscle cells, with the subsequent development of uterine fibroids.

TABLE I

	Cases
Type of first operation	
Dilatation and curetage	44
Application of radium	8†
Suspension of uterus	10*
Unilateral salpingo-oophorectomy	10*
Abdomen opened in 20 cases 45 per cent of total	
† Number of hours undetermined	
Condition of ovaries at first operation	
Diagnosed microscopically as cystic	10
Diagnosed operatively as cystic	6
Not mentioned at operation	4
Curettements	
Abundant	16
Polypoid	8
Moderate	8
Small	5
Not mentioned	7
Time interval between operations	
Longest	13 years, 2 months
Average	4 years, 9 months
Shortest	1 year, 2 months
Type of second operation	
Hysterectomy	44
Bilateral salpingo-oophorectomy	18*
Removal of all remaining ovarian tissue	10*
Unilateral salpingo-oophorectomy	16
All ovarian tissue removed in 28 cases 64 per cent of total.	
Condition of myometrium (microscopic)	Cases
Fibromyomatous	44
Hyperplastic	24
Fibrotic	6
Adenomyomatous	8
Normal	14
Malignant	1
Condition of endometrium (microscopic)	
Hyperplastic	40
Premenstrual	4
Condition of ovaries at second operation (microscopic)	
Multiple follicle cysts	44
Corpus Luteum	
Mature	4
Degenerating	5
Absent	35
Miscellaneous	
Salpingitis	18*
Adhesions	20*
Ovarian endometrial transplants	22†
* 38 cases, 86 per cent of total	
† 50 per cent of total	

#### ENDOMETRIOMAS

Endometriosis is a term introduced by Sampson to include a variety of adenomatous lesions of the female pelvis, the histological and functional characteristics of which are identical with those of the endometrium. The

etiology of endometriomas is still a matter of debate. Up to the present we must offer thanks (1) to Cullen for the mucosal or diverticular origin of the diffuse uterine growths (2) to Ivanoff for his serosal theory which draws attention to the proliferative potentialities of the peritoneal mesothelium (3) to Sampson (26) for the hypothesis of tubal regurgitation or retrograde menstruation theory with direct implantation of living endometrial grafts and (4) to Robert Meyer (24) championed in this country by Novak, for his invaluable demonstrations of epithelial heterotopy and metaplasia which helps to render more intelligible many extrapelvic growths of like character. Suffice it to say that at present two views are generally held as the cause of these tumors, either the cellular spill hypothesis of Sampson or the theory of serosal cell heteroplasia advocated as early as 1898 by Ivanoff. That neither one of these theories can explain the occurrence of endometriomas at all sites is generally accepted. The heteroplasia view of the serosal cell cannot explain the perineal endometriomas, while inguinal canal endometriosis is difficult to ascribe to the implantation theory of fragments of the uterine lining.

It is not the intention of this paper to enter this field of discussion and the following remarks and observations will hold good irrespective of the primary source of the endometrial elements. If the endometrioma is explained by the implantation view there must be some stimulant or environment which decides whether the endometrioma will grow or perish. Sampson (27) took cognizance of this fact and stated that the escaping cells need suitable soil. On the other hand, if the origin of the endometrioma is from heteroplasia of serosal or germinal cells, some factor must be present which first instigates the cellular change and which subsequently stimulates the endometrial growth. The actual origin of the endometrioma is unimportant, whether from implantation of a living graft or from cellular metaplasia, the all important question is the determination of the cause of the igniting factor which controls this cellular change or which stimulates to proliferation the endometrial implants.

The morphological and functional characteristics of endometriomas are similar to uterine endometrium. Its integrity and function are dependent upon the presence of active ovarian tissue since castration causes regression of the tumor. It presents decidual reaction during pregnancy. It undergoes the phases of the menstrual cycle changes dependent on the ovarian hormones and Gleave has proved that in rabbits the presence of the estrogenic principle is essential for the maintenance of the lesion.

Since the ovarian follicular hormone is the cause of endometrial hyperplasia and the histological structure of endometriomas and uterine endometrium are similar it is logical to deduce that the igniting factor of endometriomas, which brings about the cellular metaplasia or the implant proliferation is the estrogenic principle. That such is the case is all the more established by the fact that many endometriomas present histologically endometrial hyperplasia, and also by the high incidence of association of endometriomas with uterine endometrial hyperplasia. The frequent finding of all the features of endometrial hyperplasia in the endometriomas accompanied by similar changes in the uterine mucosa, can only be caused by the factor which determines the latter the ovarian follicular hormone.

In a former contribution (35) while studying the relationship between endometrial hyperplasia and uterine fibroids, the high incidence, 30 per cent, of ovarian endometrial transplants was noted. At that time the suggestion was made that these three conditions might possibly have a common etiological background. These figures have been rechecked and together with the findings in the present paper ovarian and uterine endometriomas were associated with endometrial hyperplasia and uterine fibroids in 64 per cent of the cases, a figure far too high to make such a finding mere co incidence.

Other authors have likewise called attention to the high incidence of association of these three conditions. In Jaffe's series of 123 cases of endometriomas, 79 women, 71 per cent exhibited endometrial hyperplasia, while 31 or 28 per cent, presented

fibroids in the uterus In discussing endometriosis, Allen (2) was impressed with the high incidence of association of this condition with menstrual irregularities due to endometrial hyperplasia, 70 per cent, uterine fibroids, 41 per cent, and the prevalence of relative sterility, 60 per cent The marked irregularities of the menstrual habit immediately suggested a glandular imbalance He considered that such a hypothesis more accurately explained those instances of irregular bleeding occurring in patients in whom the endometriomas were so located that they could not possibly have caused the hemorrhage Smith, in 159 cases of endometriomas, noted endometrial hyperplasia associated in 42 per cent and uterine fibroids in 52 per cent of the women Other observers, Taylor, Shaw, Beckman, Novak and Martzloff, and Tietze have reported the occurrence of these stigmas of glandular activity in patients afflicted with endometriosis

Therefore, it seems logical to deduce that the multiple follicle cysts of the ovaries, in the absence of corpora lutea, which cause, through the action of the estrogenic principle, endometrial hyperplasia, likewise cause the ectopic endometriomas Figures 1 and 2 are presented to show the similarity of the hyperplasia of the endometriums of the uterus and ovarian endometrioma Both slides were taken from the same patient

There are two clinical features common to these three conditions, uterine hemorrhage and absolute or relative sterility Functional uterine bleeding has long been observed as the clinical manifestation of endometrial hyperplasia Graves (14) and King have called attention to this same clinical feature in women with uterine fibroids which were so located that the origin of the bleeding could not possibly have come from the fibroids Their explanations are that the bleeding results from the associated endometrial hyperplasia Likewise Allen (2) offers endometrial hyperplasia as the source of the uterine hemorrhages in women with endometriomas so situated that they could not have been the cause of the bleeding

Sterility absolute or relative, is another clinical feature characteristic of these three

conditions In endometrial hyperplasia, when the patient is bleeding, absolute sterility is assured In women with fibroids, sterility runs as high as 35 to 40 per cent of the cases, while in cases of endometriomas Herd and Allen (2) place the figure around 60 per cent The explanation for the sterility in these three conditions is undoubtedly lack of ovulation, so well demonstrated in the ovaries by the presence of multiple follicle cysts and the absence of corpora lutea

### CONCLUSION

The hypothesis that all forms of overgrowth of the uterine endometrium or musculature are due to the same factor, the estrogenic principle, is not only supported by clinical and pathological data, but also explains satisfactorily the simultaneous development of endometrial hyperplasia, endometriomas and uterine fibroids, with their associated clinical features, hemorrhage and sterility

### BIBLIOGRAPHY

- 1 ALLEN, E Ovarian Follicular Hormone. Sex and Internal Secretions Chap 9, pp 392-481 Baltimore The Williams and Wilkins Co, 1932
- 2 Idem. A clinical and experimental study of endometriosis. Am J Obst & Gynec., 1933, 26 803-814.
- 3 BECHER, E Study of the histogenesis and morphogenesis of uterine myomas Ztschr f Geburish., 1916, 78 281
- 4 BECKMAN, M Hyperplasia and hypertrophy of the uterine mucosa. Arch f Gynaek., 1929, 135 519-535
- 5 BURCH, J C, et al Etiology of endometrial hyperplasia. Surg, Gynec & Obst., 1931, 53 338-345
- 6 Idem Endometrial hyperplasia. Arch. Path., 1934, 17 799-826
- 7 CLAUBERG, C Artificial growth of human uterus Zentralbl. f Gynaek., 1933, 57 1991-1996
- 8 CORNER, G W The relation between menstruation and ovulation in the monkey its possible significance for man. J Am. M. Ass., 1927, 89 1838
- 9 CULLEN, T S Adenomyomata of Uterus. Philadelphia W B Saunders & Co, 1908
- 10 DESNOO The regeneration of uterine mucosa J Obst. & Gynec Brit. Emp, 1934, 41 568
- 11 FLUHMANN, C F The significance of the anterior pituitary hormone in the blood of gynecologic patients Am J Obst. & Gynec., 1930, 20 1
- 12 Idem. Hyperplasia of the endometrium and the hormones of the anterior hypophysis and the ovaries. Surg, Gynec. & Obst., 1931, 52 1051-1068
- 13 GLEAVE, H. H. On the growth of endometrial transplants in the rabbit. J Path & Bacteriol., 1930, 33 675-681
- 14 GRAVES, W P Some observations on the etiology of functional bleeding Am. J Obst & Gynec., 1930, 20 500

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750

15. Idem. Uterine Myomata. *Curtis System of Obstetrics and Gynecology*. Vol. 2, pp. 747-833. Philadelphia and London: W. B. Saunders & Co. 1913.
6. HELLMANN. The origin of myomata. *Ztschr. f. Geburtsh.* 9 6, 88 713.
7. HERR, S. B. Endometriomata, abnormal development of endometrial tissue in the female pelvis. *J. Obst. & Gynec. Brit. Emp.* 925, 3 649.
8. I. WERT, V. S. Adenomyomata of the uterus. *Monatschr. f. Geburtsh. Gynec.* 898, 7 292.
9. JEFFCOATE, T. M. A. Endometriosis as manifestation of ovarian dysfunction. *J. Obst. & Gynec. Brit. Emp.* 934, 41 684-707.
20. KIRBY, J. E. Endometrial hyperplasia and its relation to endocrine dysfunction. *Am. J. Obst. & Gynec.* 933, 36 583-587.
- LEWIS, D. and GERSHBERGER, C. F. Gonadotropic and estrogenic principles in myomas of the uterus. *J. Am. M. Ass.* 935, 64 45-46.
2. MEYER, R. Normal and pathological evolution. *Arch. f. Gynec.* 930, 93 59-1 5.
3. Idem. The Pathological Anatomy of the Uterus. Chap. 7, P. 3.
24. MEYER, R., and KRELL, L. Endometrial adenomyosis and aberrant cells. *Zentralbl. f. Gynec.* 924, 48 1449-1460.
5. NOVAE, E. and MARTILOFF, K. H. Hyperplasia of the endometrium, clinical and pathological study. *Am. J. Obst. & Gynec.* 924, 8 389-41.
26. SAUNDERS, J. A. Proliferating hemorrhagic (chocolate) cysts of the ovary their importance and especially their relation to pelvic adenomas of endometrial type. *Arch. Surg.* 9 4, 3 445.
7. Idem. Benign and malignant endometrial implants in the peritoneal cavity and their relation to certain ovarian tumors. *Surg. Gynec. & Obst.* 924, 38 187-3 1.
28. SCHNODDER, R. Anatomical study of the normal and pathological physiology of menstruation. *Arch. f. Gynec.* 9 5, 27 22.
29. SEAW, W. Irregular uterine hemorrhage. *J. Obst. & Gynec. Brit. Emp.* 929, 36 1-69.
30. SMITH, G. V. Endometriosis. Clinical and pathological study of 59 cases. *Am. J. Obst. & Gynec.* 929, 7 808.
3. TILLOT, H. C. Jr. Endometrial hyperplasia and carcinoma of the body of the uterus. *Am. J. Obst. & Gynec.* 932, 3 309-312.
1. TUCKER, A. Clinical and anatomical studies of ovarian tumors. *Arch. f. Gynec.* 93 38 97-111.
28. VAN HANDEL, M. Contributions to our knowledge of the menstrual cycle. *Monatschr. f. Geburtsh. u. Gynec.* 906, 24 799.
24. WILKINSON, J. T. A possible cause of uterine fibroids. *Endocrinology* 933, 7 793-798.
23. Idem. The interrelationship between ovarian follicle cysts, hyperplasia of the endometrium, and fibromyomata. *Surg. Gynec. & Obst.* 933, 56 226.
36. Idem. The etiology of uterine fibroids, with special reference to the frequency of their occurrence in the negro. *Surg. Gynec. & Obst.* 934, 58 57.
27. ZONEN, E. The relation of the anterior lobe of the hypophysis to genital function. *Am. J. Obst. & Gynec.* 934, 24 836.
38. Estrogenic substances. *Theoria. J. Am. M. Ass.* 933, 60 33 338.



HISTOLOGICAL STUDIES OF ENDOMETRIUM DURING  
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WHILE the essential features of the menstrual cycle have been recorded by many observers, there is a distinct lack of correlation between the observed state of the endometrium and the clinical picture. Further, no unity exists in the present system of reporting the several phases of the cycle. The object of this study was to attempt to clarify this seemingly chaotic state and to present some of the newer conceptions regarding the regenerative phenomena that occur in the menstrual cycle.

Present knowledge concerning the menstrual cycle may be stated briefly as follows. Westphalen, in 1896, was probably the first to study the endometrium in relation to the menstrual cycle. Although his work was done with material obtained at necropsy and under some technical handicaps, it nevertheless was of some consequence. Westphalen believed that regeneration of tissue was complete by the fourteenth to fifteenth day, he did not, however, give any results to support this belief.

The next notable contribution was made in 1908 by Hirschmann and Adler who studied uteri removed during the menstrual cycle. Their work is accepted today, with some modifications, their records, however, were incomplete, especially regarding the menstruating or "tissue loss" phase, and this information was supplied by the excellent observations of Schroeder in 1915. Novak and TeLinde (22), in 1924, reported a study corroborating the results of Schroeder. The material for this study was collected in such a way as to eliminate possible errors of technique which had been responsible for misinterpretation in many previous studies. The outcome of these observations was the classification of the cyclic changes in the endometrium as follows: (1) postmenstrual phase, (2) interval phase (called by some, resting endometrium), (3)

pregravid or premenstrual phase, and (4) menstruating endometrium. This classification is accepted and used by most workers in this country at the present time. Novak (23) subscribed to this classification and recently has described each phase.

A few significant facts concerning the nature of the process under study also deserve mention. Zeleny, in 1916, in a study of regenerative phenomena under normal conditions, observed certain phases: (1) a phase of regulation, which was characterized by reorganization and migration of cells in the area of "tissue loss," (2) a phase of cellular proliferation, which was characterized by mitosis and a rapid increase in the size of the regenerating area, and (3) a phase of cell and tissue differentiation, which was accompanied by decline in cellular proliferation and by an increase in the size of the regenerating area. The regulative phase lasts for approximately 48 hours, the proliferative phase then follows and reaches a maximum in 7 to 10 days, this is then followed by the differentiative phase, which reaches a maximum in about 18 days, when the increase in size of the regenerating area has about ceased. Differentiation is characterized by the change into the definitive or functioning tissue. This work was checked by Speidel, in 1929, and he observed the same phases. In 1933, Herrell observed similar results in the regeneration of tissue as a result of pituitary stimulus, and while these studies were not of human tissues, it seemed to us that the same basic principles might well hold for regenerating tissues of any type. With this in mind, we at once sought a human tissue suitable for such studies. Interestingly enough, the endometrium is unique in that it, in a cyclic fashion, undergoes "tissue loss" which is followed by the phenomenon of complete regeneration.

<sup>1</sup> Abridgment of thesis submitted by Dr. Wallace E. Herrell to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

With these facts in mind the present study was undertaken to apply these principles of regeneration, if possible, and to correlate the observed states of the endometrium with the basic physiological principle at work in the process.

#### MATERIAL AND METHOD

Material for this study was obtained from the operating rooms of the Colonial Hospital and it was examined in the laboratory of surgical pathology under the supervision of Dr Broders. Portions of more than 241 specimens of endometrium were prepared by the frozen section method of Wilson as modified by Broders, and such specimens were stained with Terry's neutral polychrome methylene blue. Portions of 160 of these specimens of endometrium were prepared for study by the fixed frozen section technique, and these were stained with hematoxylin and eosin. Data were obtained in each case from the clinical record and from the individual patient. By this means, specimens were observed during every phase of the menstrual cycle and were obtained from whole uteri or from scrapings secured in the course of dilatation and curettage. Fifty-two specimens were obtained by the use of the instrument recently described by Randall.

#### EXPERIMENTS AND OBSERVATIONS PHASES OF THE CYCLE

**Menstruating phase.** Five specimens were obtained during the phase of "tissue loss," and according to the observations made there can be no doubt that loss of tissue is complete in the first 24 hours of menstruation and is one of the remainder of the menstrual period. This observation is in accord with observations made by Novak and others. Some observations, however, do not concur in this view. Figure 1 illustrates the loss of tissue. The specimen was obtained 24 hours after the onset of the menstrual period of a patient whose cycle corresponds approximately in three-fourths of the endometrium there remains only the basal layer of endometrium, which measures approximately 0.5 millimeters. This picture might

well be confused with that of a freshly curetted uterus. The glands in the basal layer remain essentially the same throughout the cycle; hence, one can learn very little concerning the phase from such specimens when obtained either by dilatation and curettage or from the whole uterus. The surface and outer layer of endometrium however afford means of determining the phase of the menstrual cycle accurately although this is as easy to determine from specimens removed at dilatation and curettage as it is from a block from the whole uterus, assuming the sections are prepared properly. The small layer of endometrium should be noted (Fig. 1). Of particular significance also is the height of the epithelium and the general configuration of these glands. Figure 2 illustrates the difference between the histological structure of the basal epithelium and the epithelium of these glands. The latter epithelium remains essentially the same throughout the cycle. The term "sub-basal" has been proposed for these glands, to which reference will be made later in this paper.

**Early reparative phase of migration and rearrangement of cells.** The next 24 hours of the menstrual cycle are taken up with reorganization, rearrangement and migration of cells. From microscopic study one is able to learn that the cells lining the remaining glands will take part in resurfacing the endometrium. Mitosis is not active in fact, this phase is similar to the early phases observed before by Zelensky Speldi and Herrell in the study of regenerating tissues. No evidence has been collected in this study in support of the theory of metaplasia of the stroma in remaining endometrium. In fact glandular tissue seems the most likely source of the resurfacing epithelium.

**Early proliferative phase (first 24 hours day).** This phase corresponds roughly to that previously and we believe incorrectly called the postmenstrual phase. It is characterized by active division of cells, resurfacing of the endometrium and formation of new straight tubular glands from the surface epithelium (Fig. 3). Mitosis is active and cellular proliferation occurs also in the loose embryonal



Fig 1 Menstruating phase ("tissue loss") Specimen obtained 24 hours after onset of menses in a normal cycle. Note subbasal glands and loss of outer two layers of endometrium. Stained with hematoxylin and eosin ( $\times 35$ )

type of stroma. By the end of the first week in this phase, the endometrium presents a fairly typical picture. The average number of glands per low power field is three to four, and these glands are nearly straight tubules, the epithelium of which is of moderately low columnar type, with nuclei situated near the center of the cell. The endometrium grossly is from 1 to 1+ millimeter in thickness. One may therefore at once state the time of the last period and hence the phase of the new cycle. One should always study these glands, if possible, in the longitudinal view, if they are



Fig. 2 Left, a photomicrograph of the epithelium of the basal gland at a high magnification to be compared with figure at right. This illustrates typical late differentiative phase in contrast to the inactive epithelium of the subbasal gland. Stained with hematoxylin and eosin ( $\times 140$ ). Right, Subbasal gland. Photomicrograph at same magnification as figure at left to illustrate difference in height of epithelium.

seen on cross section, however the phase is discernible by the characteristics just outlined. The tubular glands will appear in cross section merely as small circles, with other features of the early proliferative phase (Fig 4).

*Late proliferative phase (eighth to fourteenth day)* This phase corresponds roughly to what has previously been called interval or resting endometrium, and it is with this phase that we especially wish to deal. The regenerative phase here is *not* a resting endometrium nor is there such a phase. The very nature of the



Fig 3 Early proliferative phase. Specimen obtained on the sixth day in the normal cycle in a young patient. Straight tubular glands, three per low power field; mitosis active. Gross measurement 1 millimeter. Stained with hematoxylin and eosin ( $\times 50$ )

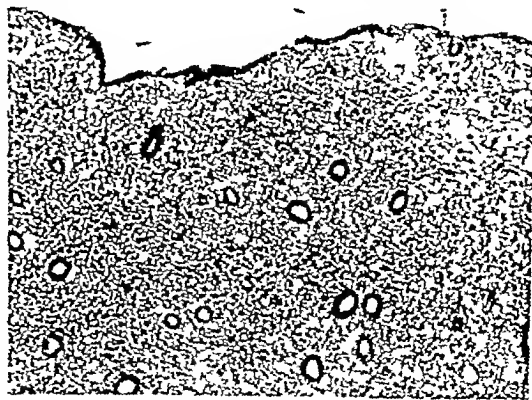


Fig 4 Early proliferative phase (cross section). Specimen obtained on fifth day of cycle illustrating early proliferative phase when glands are seen on the cross section only. Other features similar to early phase. Stained with hematoxylin and eosin ( $\times 35$ )

TABLE 1.—ANALYSIS OF 188 CASES IN WHICH A DIAGNOSIS OF HYPERTROPHIED ENDOMETRIUM WAS MADE

Phase	Days	Cases	Glands per low power field	Average thickness of endometrium, mm.
Early proliferation	to	24		—
Late proliferation	2 to 24	24		
Early decidualization	to	24	6 to	
Late decidualization	to 26	60	to 7	
Menopausal and postmenopausal		26		
Total		138		

(1921-21) later popularized the term. In fact, Novak is greatly responsible for its widespread use. Novak (20) however recognizing the difference between the so called hypertrophy and what he thought to be another entity introduced the term hyperplasia. The microscopic picture of hyperplasia he described as small tubular glands associated with dilated areas lined with flat epithelium. These cyst like areas have been said to be pathognomonic of hypertrophy. The significance of this statement will be considered later. suffice to say however the observations made here will not support this theory. In a study of 159 cases in which the endometrium was removed before the fourteenth day of the menstrual cycle, the diagnosis of hypertrophy was made only once by Novak. This is but further proof that the differentiative phase in the menstrual cycle has been repeatedly confused with hypertrophy. In this same series of cases, the diagnosis of hyperplasia was made several times by Novak but always in cases in which there was a climacteric history and in which the patients were more than 40 years of age.

Others, as well as Novak, said that there could be no bleeding without hyperplasia however time has tempered to a great extent this view. Excellent contributions by Inpach (1934), Suggs (1934), Hartman as well as others offer ample theoretical evidence to refute any relationship between the so called hypertrophy or hyperplasia and the clinical intensity of menstruation.

To clarify this confusion we would like at this point to define the terms "hypertrophy" and hyperplasia from standard medical dictionaries. Hypertrophy may be defined as the morbid enlargement or overgrowth of

an organ or part. Likewise "hyperplasia" may be defined as the abnormal multiplication or increase in the number of tissue elements. It is obvious therefore that the use of these terms as descriptive pathological terms is entirely misleading and without substantive histological support.

As a test of the significance of such a diagnosis, a careful study was made of sections prepared from 188 specimens from which a diagnosis of hypertrophied endometrium had been made in this department. The clinical history was not consulted until the phase of the cycle had been determined according to the criteria proposed in this report. A careful analysis of the data obtained reveals no justification for such a diagnosis without qualification. Reference to Table I will indicate the experimental basis for the facts which have been stated.

Interestingly enough the diagnosis was made more frequently in the late phases of the menstrual cycle than it was in the early phase however the diagnosis not infrequently has been made from specimens measuring 1 millimeter in thickness, specimens containing three glands per low power field, and specimens presenting all the characteristics of early proliferative endometrium. These do not represent selected specimens they were surgical specimens, routinely diagnosed as hypertrophied endometrium in 188 consecutive cases.

#### CYSTIC ENDOMETRIUM

Reference has been made to the appearance of cystic areas occurring in endometrial specimens, which are often diagnosed as hypertrophied endometrium. This is an error caused by faulty interpretation of these cystic areas, which accompany clinical ovarian failure or



Fig 9 Left, Subbasal glands Specimen showing subbasal glands 1 millimeter below the surface epithelium in a fetus, 30 weeks of age. Stained with hematoxylin and eosin ( $\times 35$ ) Right, Subbasal glands (so called internal adenomyosis) Specimen obtained from menstruating uterus of a girl 15 years of age, showing normal cycle. Note subbasal glands which are said to occur only at menopause Stained with hematoxylin and eosin ( $\times 35$ )

the approaching menopause rather than an associated hyperplasia

This picture has been described by some as the "swiss-cheese" endometrium, however, we propose the term "cystic endometrium" and would point out its significance. During this study, cystic areas have been observed in approximately sixty endometrial specimens, none of which could be classed as hypertrophied endometrium. In all cases there has been clinical evidence of ovarian failure or approaching menopause. The occurrence of these areas in the endometrium of a patient even with a normal cycle, heralds the approaching menopausal age with such consistency that one usually can predict without the clinical data the approximate age of the individual. Shaw, Graves<sup>(14)</sup>, Cannon and more recently, Duhig, have postulated, without experimental support, that this "cystic hyperplasia" is often associated with ovarian (follicular) dysfunction. Likewise Burch in a study of so called endometrial hyperplasia has reiterated the fact that corpora lutea are not present in the ovaries of patients who come to operation suffering with "cystic glandular hyperplasia and in fact the ovaries are generally cystic." This

is a pertinent observation. Since the work here presents substantive histological evidence that the secretion of the corpus luteum has to do with differentiation (previously called pre-gravid endometrium), and since this phase is admittedly the picture called by most workers hypertrophy, it becomes obvious that such a diagnosis is incorrect. Rather the histology is one of arrested regenerative phenomenon in an early phase and the cysts result from failure of the ovarian tissue. Cystic areas associated with arrestment of the regenerative process will be discussed later. Figure 8 illustrates a typical example of the cystic endometrium of a patient whose cycle is still normal, but who without question is approaching the menopausal age. Cystic areas have been observed also in young patients whose endometrium was not hypertrophied according to gross measurements or microscopic examination but who presented clinical syndromes of ovarian failure. The practical significance of this observation is obvious as regards therapy.

#### SUBBASAL GLANDS

Attention is again called to the small glands for which we have proposed the term "sub-



Fig. 24. Persistent late differentiative phase. Specimen removed from patient aged 26 years. Regular irregularly 11th menstrual interval from 1 to 4 months for past 3 years. Last menstrual period 3 months before her admission to hospital. Specimen identical 11th late differentiative phase (see Fig. 7). Stained 11th hematoxylin and eosin ( $\times 25$ ).



Fig. 3. True atrophic endometrium. Specimen of uterus removed several years after removal of both ovaries. Endometrium similar to perimenstrual type. Single layer of epithelium overlies loose stroma. 11th few non functioning basal and subbasal glands. Stained 11th hematoxylin and eosin ( $\times 60$ ).

abeyance. Fluhmann (1932) in a very painstaking study observed that the ovaries of patients with hyperplasia (usually just before and during the menopause) characteristically showed ripening follicles with complete absence of mature corpora lutea. Thus, there was a complete absence of the influence of progesterin. It is logical, therefore to reason from these observations that the several observers have described a state of the endometrium which is the result of ovarian failure to the degree of absence of the hormone of the corpus luteum. Since these observations rather conclusively

demonstrate that differentiation of the endometrium is dependent on this hormone it becomes obvious that the regenerative process will proceed only to that point controlled by the follicular hormone and will proceed no further when activity of the corpus luteum is absent. This results in a persistent proliferative phase and not in hyperplasia. The endometrium usually does not measure in the gross, more than 1 to 2 millimeters at any time. There are three longitudinal glands per low power field and the epithelium is of the low proliferative type. All of these features are further evidence that this condition is not a hyperplasia. In this study 16 specimens of this type of endometrium have been collected from patients who presented typical menopausal symptoms and from patients who had symptoms of amenorrhea.

*Persistent late proliferative phase.* Similar to patients seen in the first phase of the menstrual cycle there are cases in which the regenerative process progresses to a point further in the cycle and becomes arrested at this point. Figure 2 is a photomicrograph of a section of endometrium removed from a patient aged 23 years, who had oligomenorrhea (in this case menstruation occurred 3 to 6 months with occasional moulins). The last menstrual period had occurred 3 months before her admission to the clinic. This section illustrates a



Fig. 6. True atrophic endometrium. Small islands of epithelial cells in loose stroma. Stained 11th hematoxylin and eosin ( $\times 80$ ).

typical late proliferative phase of the menstrual cycle, that is, there are approximately six longitudinal glands per low power field. These glands are somewhat dilated but straight. The histological appearance of this section presents nothing which would indicate deviation from the normal, however, from the history, it must be called a persistent proliferative endometrium. This indicates a deficiency of corpus luteum, that is, the stimulus for regeneration is present in sufficient quantity to bring about complete proliferation, but differentiation is lacking and hence menstruation does not occur. From a therapeutic standpoint, this observation is of great importance in supplying the necessary deficient hormones.

*Persistent early differentiative phase* Examples of endometrium have been encountered which are definitely in a persistent differentiative phase. Figure 13 illustrates the endometrium of a young woman who had had irregular menstrual periods for 2 years. There had been an interval of 3 to 6 months and an occasional molen. This specimen is typical of the early differentiative phase. There are six glands to the low power field, some increase in the height of the epithelium, and evidence of beginning convolution of the glands all of which are characteristic features of early differentiation. The condition illustrated by this section should respond to ovarian stimulation, which in turn should bring about differentiation, thus completing the process of regeneration.

*Persistent late differentiative phase* Cases have been seen in which histological study revealed a very slight ovarian deficiency, or at least a lack, of the factor which would initiate the menses. Figure 14 is a section of endometrium removed from a young woman whose menstrual periods had occurred at intervals of 3 to 4 months, however, there always had been a definite molen at the expected date. This section shows a typical late differentiative phase of the menstrual cycle. There are six or seven longitudinal glands per low power field, the glands are twisted on the longitudinal axes, and the epithelium is of the tall columnar type. The nuclei are displaced toward the base of the cell. The gross measurement is between 3.5 and 4 millimeters. It is, therefore,

reasonable to say that this is an example of a persistent late differentiative phase. In light of the foregoing observations, it may be assumed that slight ovarian stimulation should be sufficient to bring about a readjustment in the cyclic regenerative changes in this type of endometrium.

#### ATROPHIC ENDOMETRIUM

The term "atrophic endometrium," like the term "hypertrophic endometrium," has been used rather loosely. It has been applied to menopausal as well as postmenopausal endometrium, however, observations made in this study would indicate that true atrophic endometrium would be more applicable to that type of endometrium in which complete and rather sudden ovarian failure has occurred. Following sudden failure (either spontaneous or artificial failure, such as occurs after surgical removal of the ovarian tissue), there occurs a lack of both the follicular hormone and the hormone of the corpus luteum, which are the stimuli to endometrial regeneration, and hence true atrophy occurs. The gradual failure of the ovaries incident to the climacteric usually is associated with cystic formation, as stated before. However, sudden withdrawal or failure of ovarian tissue is accompanied by a true atrophy (Fig. 15). This figure illustrates a section of uterus removed from a patient whose ovaries had been removed several years before. The remaining endometrium consists of a single layer of epithelium overlying a loose stroma. This is typical of true atrophic endometrium. In this type of case biopsy or even vigorous curettage will secure only small amounts of endometrial tissue. However, a diagnosis can be made from the presence of small islands of epithelial cells which usually are situated in the loose stroma described previously. Figure 16 illustrates a true atrophic endometrium removed from a patient aged 29 years, who had had a sudden onset of amenorrhea 12 months before her admission to the hospital. From this histological picture, it may be concluded that therapy, regardless of type or duration, probably will do little to restore this endometrium. Nine such cases have been studied, however, they serve to indicate the difference between true atrophic and the

TABLE II.—RESULTS ACCORDING TO CLASSIFICATION PROPOSED IN THIS STUDY\*

	Source of material		
	Hysterotomy	Dilatation and curettage	Biopsy†
Phases of cycle (normal)			
Early proliferative phase		5	
Late proliferative phase	26	26	
Early differentiative phase	14	39	12
Late differentiative phase	66	17	
Persistent phases of cycle			
Early proliferative phase			7
Late proliferative phase			
Early differentiative phase			
Late differentiative phase			
Cystic endometrium	14	20	6
True atrophic endometrium			4
Schmid's glands			
Postmenopausal			
Menstruating ("brown line")			
Total	201	140	32

\* Dyssected hysteromorph endometrium, 138 (about 1/3 of the specimens in this group fall in the classification of persistent phases of the menstrual cycle). The remaining 163 specimens of the hysterotomy group with the histological study in the diagnosis of endometrium of patients with symptoms which require true atrophic description. A few of these cases were studied also by the dilatation and curettage.

menopausal type of endometrium, which is usually a persistent early proliferative phase in a cystic type of endometrium.

#### ANALYSIS OF STUDY

The specific observations have been considered previously in the separate sections. An effort has been made to consider briefly the different phases of the regenerating human tissue heretofore mentioned. It becomes clear after consideration of the results following tissue loss, that they can be explained in terms of a few general basic principles at work in the regenerative process. The significance of these observations becomes obvious when one considers them in the light of an analysis of the regenerative phenomena. The different phases have been cited previously. Following injury or spontaneous tissue loss, approximately 48 hours are taken up with migration and reorganization of cells and this is the vital period in the whole process of recovery or regeneration.

Following this, proliferation goes on actively and is associated with frequent cellular division and at times, with active mitosis. This mitotic activity usually progresses rapidly until the tenth day and declines at the beginning of the third week. It is interesting that Westphalen as early as 1896 noticed that mitosis in the endometrium was most marked from the seventh to the eighteenth day of the cycle. However, he was unable to explain this observation. Likewise, Novak noted that mitosis never occurred during the loss of tissue, an observation which he also was unable to explain. In light of our present knowledge of regeneration of tissue, it becomes obvious that Novak was observing the phase of cellular migration which lead him to postulate that cellular division took place by amitosis. Likewise, Westphalen was observing the period of active proliferation which is practically completed by the eighteenth day following which the process of regeneration is one of differentiation and hence very little mitotic activity is to be observed.

Regarding the rôle played by the hormone of the corpus luteum (progestin) in the differentiation of the endometrium, one needs only to say at this time that comparative histological studies alone indicate that the rôle is very definite. A demonstration of the potency of the follicular hormone by such investigators as Allen, Delsy and their collaborators was of great aid in these studies, however too much emphasis was placed on this hormone. Hence, the discovery of the principle of the corpus luteum was delayed. At present, ample experimental proof exists to establish clearly the fact that ovulation occurs in the human being and that this usually occurs at the middle of the cycle (fourteenth to fifteenth day). This is followed by activity of the hormone of the corpus luteum and by decreasing activity of folliculin.

A consideration of the experimental evidence, however does not come within the scope of this paper. It may be noted, notwithstanding that ample histological evidence has been gathered from endometrial specimens which, when correlated with accurate clinical histories, establishes the fact that differentiation is definitely under the



control of the corpus luteum. The removal of this stimulus therefore results not in hyperplasia or hypertrophy, but in an arrestment of the regenerative process in its early phase.

Table II illustrates a complete analysis of the material studied.

### CONCLUSIONS

1. A careful histological and clinical study of 293 specimens of endometrial tissue obtained in various phases of the menstrual cycle has been presented.

2. Some new conceptions of the basic principles at work in the regeneration of human tissue have been presented, with experimental evidence to confirm these conceptions.

3. Careful analysis of the results of this study reveals the fact that one is not justified in making a diagnosis of hypertrophied or hyperplastic endometrium without qualification.

4. The practical significance of cystic areas occurring in the endometrium has been indicated, with histological evidence that this is a phenomenon indicative of physiological senility.

5. Experimental evidence we believe, presents incontrovertible evidence that the subbasal glandular tissue is not a disease process pathognomonic of the preclimacteric state but rather a definitive tissue possessing potential possibilities of activity under certain conditions.

6. The value of a histological study and classification of endometrial tissue arrested in its process of regeneration, because of a deficiency of the humoral stimuli which control this process, has been thoroughly demonstrated ("persistent phases").

7. The practical value of a differentiation between true atrophic and menopausal types of endometria has been indicated.

8. As a result of this study, the following classification is used in the diagnosis of endometria in Section B on Surgical Pathology at The Mayo Clinic.

1. Phases of cycle (normal)
  - Early proliferative phase
  - Late proliferative phase
  - Early differentiative phase
  - Late differentiative phase

2. Persistent phases of cycle
  - Early proliferative phase
  - Late proliferative phase
  - Early differentiative phase
  - Late differentiative phase
3. Cystic endometrium
4. Postmenopausal endometrium
5. True atrophic endometrium
6. Subbasal glands
7. Menstruating ("tissue loss")

### BIBLIOGRAPHY

1. ADLER. Quoted by Shaw.
2. ALLEN, EDGAR, and DOISY, E. A. An ovarian hormone. *J Am M Ass*, 1923, 81: 819-821.
3. ANSPACH, B. M., and HOFFMAN, JACOB. Endometrial findings in functional menstrual disorders. *Am J Obst. & Gynec*, 1934, 28: 473-481.
4. BRODERS, A. C. Modification of Wilson's fresh frozen section technic. *J Lab & Clin Med*, 1931, 16: 734-738.
5. BURCH, L. E., and BURCH, J. C. Endometrial hyperplasia: a review of experimental work. *Am J Obst. & Gynec*, 1933, 25: 826-833.
6. CANNON, D. J. Menstruation and menstrual disorders. *J Obst. & Gynaec*, *Brit. Emp*, 1935, 42: 88-106.
7. COLLEN, T. S. *Cancer of the Uterus*. New York: D. Appleton & Co., 1900.
8. DUNIC, J. V. The pathology of metropathia haemorrhagica: a study of one hundred and twelve cases of irregular uterine haemorrhage. *Med J Australia*, 1931, (Jan 17), 67-71.
9. FLUMMANN, C. F. Hyperplasia of the endometrium and the hormones of the anterior hypophysis and the ovaries. *Surg, Gynec, & Obst*, 1931, 52: 1051-1068.
10. FRANKL, O. Quoted by Graves (15).
11. FRANKL. Quoted by Shaw.
12. GARDNER, W. S., and NOVAK, EMIL. The endometrium and some of its variations. *J Am M Ass*, 1909, 53: 1155-1159.
13. GARDNER, W. S. Hypertrophies of the endometrium. *J Am M Ass*, 1915, 64: 1831-1834.
14. GRAVES, W. P. Some observations on the etiology of dysfunctional uterine bleeding. *Am J Obst. & Gynec*, 1930, 20: 500-518.
15. Idem. Uterine myomata (fibroids). In Curtis, A. H. *Obstetrics and Gynecology*. Philadelphia: W. B. Saunders, vol. 2, 1933, pp. 745-832.
16. HARTMAN, C. G., FIORR, W. M., and GEILING, E. M. K. The anterior lobe and menstruation. *Am. J. Physiol*, 1930, 95: 662-669.
17. HERRELL, W. E. Growth and regeneration of tissue in frog tadpoles following the administration of an extract of the anterior pituitary gland. *Anat. Record*, 1934, 59: 47-67.
18. HITSCHMANN, F., and ADLER, L. Der Bau der Uterus schleimhaut des geschlechtsreifen Weibes mit besonderer Berücksichtigung der Menstruation. *Monatsschr f. Geburtsh u. Gynaec*, 1908, 27: 1-82.
19. JEFFCOATE, T. N. A., and POTTER, A. L. Endometriosis as a manifestation of ovarian dysfunction. *J Obst. & Gynaec. Brit. Emp*, 1934, 41: 684-707.
20. NOVAK, EMIL. A study of the relation between the degree of menstrual reaction in the endometrium and the clinical character of menstruation. *Surg, Gynec, & Obst*, 1915, 21: 336-354.
21. Idem. *Menstruation and its Disorders*. New York: Appleton & Co., 1921.

2. NOVAK, EMIL, and TULLOCH, R. V. The endometrium of the menstruating uterus. *J. Am. M. Ass.* 1924, 83, 900-906.
3. NOVAK, EMIL. Cyclical changes in the genital canal. In: CURTIS, A. H. *Obstetrics and gynecology*. Philadelphia: W. B. Saunders Co. 1933, pp. 305-326.
34. IDEM. Relation of hyperplasia of the endometrium to so-called functional uterine bleeding. *J. Am. M. Ass.*, 1926, 75, 292-297.
5. RAYNALL, L. M. Endometrial biopsy. *Proceedings of the Staff Meetings of the Mayo Clinic*, 93, 143-144.
36. SCHNIEDER, ROBERT. Anatomische Studien zur normalen und pathologischen Physiologie des Menstruationsorgans. *Arch. f. Gynäk.*, 1913, 94, 57-62.
37. SEAW, WILLIAM. A study of irregular uterine hemorrhage. *J. Obst. & Gynaec. Brit. Emp.* 1929, 36, 1-40.
38. SPRENGEL, C. C. Studies of hyperthyroidism. VI. Regenerative phenomena as noted in thyroid treated amphibian larvae. *Ann. J. Anat.*, 1929, 43, 1-65.
39. SOOBS, W. D. Uterine hemorrhage: investigation and treatment. *Bull. Stuart Curdie Hosp. (Buckmond, Va.)* 1934, vol. 4, No.
30. TAYLOR, H. C. Jr. Endometrial hyperplasia and carcinoma of the body of the uterus. *Am. J. Obst. & Gynec.*, 1934, 3, 309-322.
3. TERRY, B. T. Improvement in technique and results made in examining microscopically by the razor section method 2,000 malignant tissues. *J. Lab. & Clin. Med.* 1929, 4, 50-53.
32. WARNER, J. W. Physiological and pathological changes of the endometrium. *New York M. J.* 9 2, 01, 13-14.
33. WALLER, W. H. Society proceedings of American Medical Association. *Discussion. J. Am. M. Ass.* 1908, 30, 74.
34. WENTZELER, FRIEDRICH. Zur Physiologie der Menstruation. histologische Studien. *Arch. f. Gynäk.* 1906, 53, 35-70.
35. WILSON, L. B. Staining sections of living tissues, unfixed. *J. Lab. & Clin. Med.* 1914, 40-43.
36. ZIEGLER, CHARLES. Studies on the factors controlling the rate of regeneration. *Illinois Biol. Monog.* 9 6, 3, 7-69.

AN EXPERIMENTAL STUDY OF THE EFFECTS OF CONSTRICTION OF THE GREAT VESSELS OF THE HEART<sup>1</sup>

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*"Dui talem avertite casum"*—Virgil

THE serious results of pulmonary embolism are well recognized and in the last few years have received more and more attention. The apparent increase in frequency may be due to more accurate diagnosis, although Nurnburger, after an analysis of statistics, concludes that in recent years there has been an actual increase in thrombosis and embolism, but makes the reservation that this increase is not so great that the accidental can be excluded.

Pulmonary embolism is a clinical entity usually considered as a condition to be treated prophylactically, rather than surgically. Eichelter says that only every fourth to sixth case is suitable for the Trendelenburg operation, but Nystrom believes that because of our limited experience we cannot say where the line for operability has to be drawn with regard to the length of time the pulmonary artery can remain obstructed without proving fatal.

Scheidegger, in his report of 20,779 operations, noted a general occurrence of fatal pulmonary embolism in 0.69 per cent of cases with a fatality of 4.04 per cent from this cause in the exploratory laparotomies in this group. Snell, of the Mayo clinic, says that pulmonary embolism is responsible for 8 to 10 per cent of all postoperative deaths. Any malady of such frequent occurrence and high fatality must surely cause us to search for efficient restorative measures. To treat the condition prophylactically only is to disregard a large group of cases which may well become amenable to active surgical therapy. It was with the hope of contributing in some measure to a method of giving more efficient restorative treatment that this experimental work was carried on.

## HISTORICAL REVIEW

Virchow, in 1846, was the first clearly to describe pulmonary embolism and to corre-

late the relationship between thrombosis and pulmonary embolism. He first grouped the obstruction of the pulmonary artery under four general headings. In the same year he published additional work in which he described the mechanism of occlusion of the "Lungenarterie," giving the results of his experiments on animals. He injected foreign materials and observed the secondary disturbances resulting from the obstruction of the pulmonary vessels. He reported the autopsy findings. Church, in 1892, writes concerning Van Sweisen:

As far back as 140 years ago Van Sweisen recognized that clots occurred in the vessels during the puerperium and wrote gravely of their prognosis. He even performed experiments on animals, injecting acids into the veins, and bringing about phenomena in some cases identical with what we observe in phlegmasia dolens, and in others, the severe and sudden symptoms which we know to characterize thrombosis and embolism of the right side of the heart and pulmonary arteries.

The first interest in pulmonary embolism as a surgical problem was taken by Trendelenburg after he had noticed that patients stricken with a pulmonary embolus did not die suddenly but might live 15 minutes or longer. His interest in this subject led him to carry on experiments to determine the possibilities of removal of an embolus lodged in the pulmonary artery. He reported his work before the *Versammlung deutscher naturforscher und Aerzte* in Dresden in 1907.

Trendelenburg's first work was carried out on cadavers, through a great flap on the left thorax. The pericardium was exposed by a wide pleural incision and was opened widely. A 50 cubic centimeter syringe was prepared with a two-way valve which was fitted to a cannula through an obturator with a lateral clamp. Two sutures were placed about 1 centimeter apart in the wall of the conus arteriosus at a point 1 to 2 centimeters to the

<sup>1</sup> Submitted in partial fulfillment of requirements for Degree of Master of Science in Surgery, Northwestern University, Chicago.

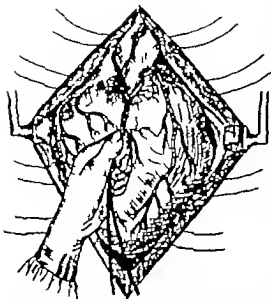


Fig. 2. This illustration shows the constriction tightened about the pulmonary artery and aorta with the common constriction of the heart which results. (After the method of Trendelenburg.)

right of the sulcus longitudinalis anterior and about 4 centimeters away from the semilunar valve. A puncture wound was made in the wall between the two sutures, with a pointed knife and the wound dilated about  $\frac{3}{4}$  centimeter. The cannula was inserted through the wound and into the conus arteriosus and the opening of the pulmonary artery. The loose embolus was then sucked out into the syringe and forced out through a lateral connection at the end of which was a small wire basket to catch the embolus.

With the embolus floating in the vessel in water in the cadaver the embolus could be caught with great agility when the heart was held. In experimental animals this was more difficult. Heparin in salt solution was used in the beginning of the operation to facilitate the passage of blood in the apparatus, no comment however being made as to its effectiveness.

At the same time he reported a trial of this operation on a 62 year old woman with a carcinoma of the colon. At operation a dense adhesion was found between the pericardium

and the heart so that the heart could not be exposed. In trying to free the adhesions a profuse hemorrhage occurred and death followed. After death, a 10 centimeter long, finger sized embolus was found in the left pleural space.

Laewen and Stevens, two of Trendelenburg's students, took up the experimental side of this problem, and in 1908 reported their results. They concluded that rabbits withstood complete interruption of the circulation for 1 minute without irreparable damage, but with compression longer than  $\frac{3}{4}$  minutes the great majority of the animals succumbed. By the use of artificial oxygen respiration, heart massage, and adrenalin they were able to get a return of heart function after constriction of the pulmonary artery and aorta for as long as 7 or 8 minutes but they found irreparable damages in the brain and were unable to obtain function from the respiratory center. A partial compression for 10 minutes preliminary to constriction had no apparent effect.

From later experiments by Trendelenburg (35) it was concluded that it was much better to incise the pulmonary artery and remove the embolus than to attempt removal by suction. In 1908, he recommended the use of special forceps for removal of the embolus and a special artery clamp for closure of the vessel.

The operative procedure which was adopted and recommended by Trendelenburg (35) was to make a T-shaped incision above the left border of the sternum and laterally over the lower border of the second rib. The second rib was resected thus immediately exposing the pleura, the costal cartilage being sectioned close to the sternum. He advised the ligation of the internal mammary artery before proceeding farther. By incision in the pleura, the pericardium was exposed and then widely opened. The Trendelenburg sound was then passed around the pulmonary artery and aorta through the transverse sinus of the heart and the rubber tube attached by means of a clip after which the tube was drawn into place. The tube was then used for a constriction of the great vessels while the pulmonary artery was incised and the embolus, located in the

pulmonary artery proper or in either the right or left branches, was extracted

From the time Trendelenburg reported his first attempt at removal of a pulmonary embolus in the human in 1908 until 1923 there were, according to Eichelter, 20 failures with the original Trendelenburg method (Capelle, Krueger, Kuettner, Laewen, Ranzi, Rehn, Sauerbruch, H. H. Schmid, Schumacher, Sievers, and Trendelenburg) before the first permanent cure was reported. These results served to show the possibilities of the operation and the technical difficulties. A few cases survived the operation for longer periods but a successful outcome had not yet been reported. Sievers had one patient survive embolectomy for 15 hours and Trendelenburg (36) had one patient live for 37 hours after operation who died of a hemorrhage from the internal mammary artery. Both of these patients were treated in 1908. Schumacher, in Sauerbruch's clinic, had a case in which patient lived 50 hours and Krueger had a patient who lived 5 days after operation to die of pneumonia. It remained for Kirschner, one of Trendelenburg's pupils, to report the first successful case in 1924.

Kirschner used the Trendelenburg technique and was able to report the only successful case to the present date in which this method was used. A. W. Meyer (21) in 1926 operated upon a patient using the original technique but he was unable to save the patient. After dissections and experiments he pointed out a new technique which was designed to overcome some of the difficulties in the older method. Meyer (21) pointed out three factors in Trendelenburg's method which served to hinder or defeat the operation and which he proposed to avoid. These factors are as follows:

(1) The opening of the pleura implies the infliction of a stupendous shock upon the already injured heart, (2) the Trendelenburg sounds and clip must be improved, and (3) the strangulation period of 45 seconds caused by the introduction of the rubber tube around the great vessels puts too much strain upon the already laboring and dilated heart (a sound heart may be able to withstand this period) and this period of strangulation evidently induces a paralysis of the respiratory centers which becomes irreparable.

The shock added because of a pneumothorax Meyer forestalled by an extrapleural approach which was secured by a wider exposure and pleural reflection in the region of the "triangle of safety." He had a sound made which was smaller and a pulmonary artery clip made shorter and narrower and covered with gauze instead of rubber. The strangulation time of 45 seconds was cut down by digital compression of the slit in the pulmonary artery after shorter intervals of work.

The technique of the A. W. Meyer modification of Trendelenburg's operation I will give in detail as he has given it.

Since one is operating upon the dying, the operation is almost bloodless. The second and third ribs must be laid bare with swift, large strokes of the scalpel. These ribs must be freed from periosteum and pleura quickly but very cautiously. The operator now gently pushes away the mammary artery and the pleura. The forefinger of the right hand is inserted to enter by way of the lower medial angle partly under the breast bone and the operator's hand gently feels its way under the insertion of the fourth rib. The pericardium, shining white and partly covered with fat, is plainly in view. Incision with the knife is followed by a flood of pericardial fluid. The pericardial cavity is laid open by introducing cautiously and energetically both forefingers which are spread out. Thus the pleura is pushed still farther out of place, and the pericardial cavity can be opened to a surprising extent.

The next step is the insertion of my modified Trendelenburg sound and the placing of the rubber tube around the artery. On the cadaver one may be in doubt as to which is aorta and which is pulmonary artery. In the living, or rather the dying, body there can be no doubt the aorta lies hidden and the pulmonary artery, swollen and pulseless, is at once visible. The Trendelenburg rubber tube is useful, as we shall presently see, not so much in strangling the vessels as in bringing the large vessels out of the depths, which may be considerable in the case of fat patients, so that they can be better observed. The pulmonary artery is incised, the tube being held lower. A quantity of blackish blood rushes out. Emboli, which may come from the heart, are also flooded out. Greater tension is now applied to the rubber tube. Forceps are placed in the right pulmonary branch, and the Trendelenburg embolus forceps is now almost horizontal. If the right branch is found to be free of emboli, a triple investigation suffices, then the incision in the pulmonary artery is grasped with the thumb and forefinger of the left hand and is pressed together. The tube at once becomes absolutely relaxed. The blood is allowed to flow through the pulmonary artery for a few seconds, when, for the first time, the tube is fairly energeti-

cally tightened, and an almost vertical, triple penetration is made into the left branch. The heart is then relieved by means of renewed digital compression of the slit in the pulmonary artery with the tube quite relaxed. Now for the second time, the tube is forcefully tightened. The left hand grasps the cranial end of the slit vessel with a pliers covered with gauze, and holds it aloft; the right hand attaches the arterial clip on the side; the tube is released. Any tightening of the tube naturally renders the work of the heart more laborious and thus injures it. The assistant must be cautioned regarding this, and must be ready instantly to obey the command, "relax, more relaxed," somewhat tighter as the case may be.

Those surgeons who have had patients survive the operations are shown in Table I.

TABLE I

Operator	Year	Time survived
Severens	1906	5 hours
Trendelenburg	906	17 hours
Kraeger	906	5 days
Schmuckner (Sawedruck Kl.)	914	30 hours
Kirschner	924	Discharged cured
Meyer	927	Discharged cured
Meyer	927	16 days
Craford	928	Discharged cured
Craford	928	Discharged cured
Nystrom	928	30 hours
Nystrom	928	5 hours
Meyer	928	Discharged cured
Meyer	928	Discharged cured
Meyer	928	Discharged cured
Nystrom	929	Discharged cured
Nystrom	929	154 hours
Marras	930	8 days
Meyer	93	Discharged cured
Westertorn	93	6 hours
Cutler	933	Unreported

There have been a total of 51 surgeons, all but one of whom have worked in European clinics, who have performed the Trendelenburg operation a total of 132 times with 19 patients who have survived the operation and 9 who have been discharged cured.

The work of A. W. Meyer (with his modification of the Trendelenburg technique) gave a great impetus to the work in this field so that 132 such operations have been reported to date, only 25 of which were done before the use of the Meyer modified technique. Elcheltzer lists 123 of these cases operated upon up to 1932 giving the surgeon and the results. Two additional cases have been reported by Griswold in this country and more recently Cutler and his associates have operated upon

and reported 7 cases in which embolectomy has been performed. In 1932 Meyer (23) was able to report his fourth successful embolectomy out of 16 reported cases. Nystrom has made contributions to this procedure by modification of the instruments used previously and construction of a triple suction apparatus. He modified the Trendelenburg sound of Meyer so that the tube when clipped into the sound would not slip out as some operators had experienced and he also has modified the pulmonary artery forceps. Nystrom used his suction apparatus successfully in extraction of large clots which could not be readily removed with the forceps. Meyer (22) has recently used a clamp for holding the pulmonary artery that is angulated.

#### THE PROBLEM

In the present method of performing pulmonary embolectomy the duration of constriction must be so brief as to be a serious handicap. The results of too prolonged constriction have been marked by deterioration in the vital centers of the brain. It has been rather generally accepted that these deteriorations in the vital centers are due to ischemia.

The original concept of this problem was based on the fact that when the arterial blood supply to a part is interrupted or seriously impaired the viability of the affected part is greatly dependent upon the amount of blood which can be retained in the vascular bed. The first observation on this point was made by Sir George Mackenzie, about 1913 from his experience in the Boer War when he noted the occurrence of a high percentage of gangrene when proximal ligation was done for arteriovenous aneurysms or aneurysmal varices while quadruple ligation and excision of the aneurysm was followed by good results. In 1913 W. A. Oppel reported marked improvement in 6 cases of senile gangrene in which he ligated the popliteal vein. In 1917 Van Kead after doing some animal experiments, recommended concomitant vein ligation to retain the blood supply in longer contact with the tissues. McNeely noted circulatory improvement in threatened gangrene of the extremities following main vein ligation. Some of the patients showed only temporary im-

provement but there occurred a noticeable decrease in pain and paresthesias following operation

It seemed a logical hypothesis that an interruption of the circulation by constriction of the great vessels of the heart on the venous side would cause a stasis in the vascular bed of the medullary and higher centers and thus protect the most vulnerable spot when the circulation is completely interrupted. Death of the respiratory center has been demonstrated in the case of embolectomy done by Nystrom who was able to get a heart beat for 7 minutes following constriction, but respiration was never resumed. Ranzi had a similar case with the heart beat lasting for 40 minutes. Kirschner was able to get a heart beat for 2 hours with artificial respiration but with complete failure of the respiratory center.

The classical experiments of Laewen and Sievers have shown that the heart can withstand blocking of the circulation for longer periods than the brain and medullary centers. The example of the effect on the brain as shown by Kirschner's successful embolectomy may be cited. Following the operation the patient was alternately delirious and comatose for 4 days before regaining consciousness. In Crafoord's first successful case the patient was unconscious for several hours, was cold and clammy, and for 2 days lay in a shock-like condition with complete amaurosis and was at times delirious. On the third day her sight returned and no cerebral symptoms followed.

An attempt was made to demonstrate a prolonged viability and more rapid resumption of activity of the medullary centers by developing a practical method of constriction of the superior vena cava. By the retention of venous blood in the brain, which we know to have a prolonged nourishing effect, it was hoped a better circulatory balance could be maintained during the period of interruption of circulation.

It is interesting to note that venous blood returned from the brain has a much higher oxygen reserve than does venous blood returned from the limbs. The nourishing effect from maintaining venous blood in contact with the tissues would accordingly be most effective in the brain. Howell has gathered

varying reports concerning the oxygen content in volumes per cent of blood in arterial and venous states but gives them as

	Vols. per cent
Arterial blood	20
Venous blood	12
Venous blood from limbs (femoral)	6.34
Venous blood from brain (torcular)	13.49

In certain anemic persons the oxygen capacity of blood may be as low as 6 to 7 per cent, owing to the reduction in the amount of hemoglobin. If the tissues take up 55 volumes per cent of oxygen, the blood enters the veins in a state of almost complete oxygen unsaturation. The large oxygen reserve in normal blood available to the respiratory center if the blood may be kept in contact with it during the time of suspended animation, should have a beneficial influence on its viability.

One might question the explanation of the failure of the respiratory center on the basis of ischemia when one considers the fact that it is easy to demonstrate early dilatation of the right auricle following occlusion of the pulmonary artery. One would reasonably conclude that such evident dilatation of the right auricle would produce sufficient passive congestion in the superior vena cava to insure against early ischemic changes.

It is probably not inconsistent to suggest that this apparent discrepancy can be explained by assuming that the inferior vena cava will accommodate so large a proportion of the total blood volume without material increase in its intravascular pressure that the superior vena cava will not reach a state of sufficient pressure to insure widespread resistance to the rapid emptying of the minute arterial capillaries until irreparable damages to such centers as the respiratory center have resulted.

A further explanation of the inadequacy of the back pressure in the superior vena cava is based on the fact that the hydrostatic pressure necessary to dilate the auricle with its very thin wall is not adequate to produce sufficient intracaval pressure to insure its retrograde distribution through lumen decreasing tubes to the capillary bed. This is in

accord with the principles of the hydraulic gradient (20)

From this we may infer that two important purposes may be served by occluding the vena cava at its entrance into the auricle. First, the auricle will be relieved from its distending pressure, and second, each vena cava will be individually isolated and occluded to the end that its retrograde filling will more rapidly and completely retard the emptying of the arterial capillaries.

With the first experiments which were performed, it was obvious that, with present methods of constriction of the pulmonary artery and aorta, there are several serious handicaps, the results of which might well be overcome if it were possible to interrupt all circulation on the venous side in contrast to the blockage on the arterial side of the heart.

The most obvious insult at first apparent is the enormous distention of the right heart which occurs with the application of a temporary ligature to the pulmonary artery and aorta. The heart dilates rapidly when such a constrictor is applied. The rate increases at first the force is greater the heart seems to churn the blood and with each beat grows larger. The distention of the right ventricle and auricle then occurs, thus filling them to an enormous size with dilatation of the venae cavae. Extra systoles appear and the rhythm soon becomes very irregular. Gradually the force of the contractions weaken, the rate slows, and the heart stops in complete diastole.

The amount of force necessary to hold a constrictor on these vessels against the heart action of a normal dog is surprisingly great just as in any other muscle which has become fatigued by its contractions, this point is reached much sooner in the muscle which is stretched. The recovery phase of a fatigued muscle is greatly prolonged by continued efforts at contraction. Physiologically as was first shown by Bowditch, we know that the contractions of the heart muscle are always maximal. They will be more quickly exhausted against an obstruction than a skeletal muscle which does not always respond with its greatest effort. We would expect to find that the heart muscle which had been ex-

hausted by such a method would respond poorly to stimuli. It seemed logical, therefore, to propound that obstruction to the venous return to the right heart would prevent the extreme exhaustion of the myocardium as described and allow the normal rhythm of the heart to continue. This should favor the prompt recovery of the normal heart.

The physiological effect of distention of the right auricle was first shown in part by the work of Gaskell in dividing the auricle of the turtle heart into strips and then demonstrating that stretching of the auricular musculature greatly slows and finally inhibits the conduction of an impulse from the sino-auricular to the atrioventricular node.

More recently Lundy and Woodruff have clearly demonstrated the effect of right auricular distention by inserting a balloon into the auricle and distending the balloon under controlled pressure. They demonstrated that with intra-auricular pressures of 15 to 60 millimeters of mercury there was a gradual lengthening of the P R. interval from 0.08 second to 0.3 second. A period of 2.7 heart block, establishment of an independent ventricular rhythm and finally complete suppression of the P wave occurs.

After release of the intra auricular pressure there was a gradual return to the control type of sinus rhythm with normal P R. intervals.

Any increased auricular pressure directly affects the transmission of impulses from the sino-auricular node to the auricular ventricular node through the media of the auricular musculature. It would seem logical therefore, that the degree of cardiac irregularity will be directly proportional to the extent and duration of cardiac distention. Any prolongation of this interfering mechanism will undoubtedly prolong the time of recovery.

To obstruct the venae cavae would not only prevent an increase in the distention which had already occurred from interference with egress through the pulmonary artery partially occluded by an embolus but following incision of the pulmonary artery there would occur a relief of right heart distention. This relief should facilitate the return of right heart musculature to a more normal potential.



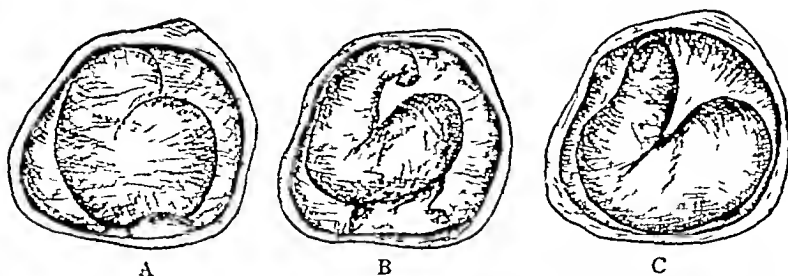


Fig. 2 Schematic drawings of stages in the development of the human heart A (After Mall), 2.0 millimeters. B and C (After His), 2.2 millimeters and 3 millimeters. (From Arey's *Developmental Anatomy* Courtesy, W B Saunders Company)

This hypothesis is supported by the distention experiments of Lundy and Woodruff

After holding a constrictor around the two great arteries and realizing the pull necessary to stop the blood flow from an actively beating heart, it is easy to understand why the intima of the pulmonary artery and even the pulmonary artery itself has ruptured in certain cases in doing a pulmonary embolectomy. When the heart action has been strong this has happened in cases operated upon by Nystrom and also by Sauerbruch, the result being a subsequent thrombosis of the pulmonary artery and loss of the patient, or an uncontrollable hemorrhage from rupture of the artery. Such fatal results from otherwise successful cases would be unnecessary if it were possible to apply constriction on the venous side of the heart where the lightest force might control the flow of blood without danger to the vessels or the heart from pressure of the constriction.

Therefore it was concluded that if a method could be demonstrated whereby the interruption of the circulation might be made on the venous side of the heart we might expect the following results

- 1 The time of interruption of the circulation might be safely prolonged

- 2 Irreparable damages of the heart and brain should occur less frequently

- 3 Distention of the right heart which occurs from obstruction of the pulmonary artery would be relieved

- 4 Heart block or the arrhythmias occurring from right auricular distention could be avoided

- 5 Following incision of the pulmonary artery in doing an embolectomy, the right heart distention could be relieved and the normal cardiac rhythm be continued or regained

- 6 Recovery time for resumption of heart function following constriction should be reduced

- 7 The danger of rupture of the pulmonary artery would be avoided

#### EMBRYOLOGY OF THE HEART

The embryological development of the heart is of particular interest in this problem. To know the route of development by which the sino-auricular node comes to its final location will perhaps more clearly visualize for us the reason for interference in the conduction mechanism which occurs from distention of the right auricle. The evagination of the aortic bulb to form the ventral aorta and the pulmonary artery from a common origin also shows us why the transverse sinus comes to be so conveniently located in relation to our particular problem. Therefore we will consider the embryology of the heart in some detail.

As given to us by Arey's *Developmental Anatomy* the heart of the lower fishes and Amphibians develops directly within the ventral mesentery of the foregut, and the mesenchymal cells differentiate directly into endo-myocardial and epicardial layers. Early heart development in lower forms such as fishes, reptiles, and birds is more complex.

The mesodermal elements very early appear between entoderm and splanchnic mesoderm and the elements arrange themselves into two

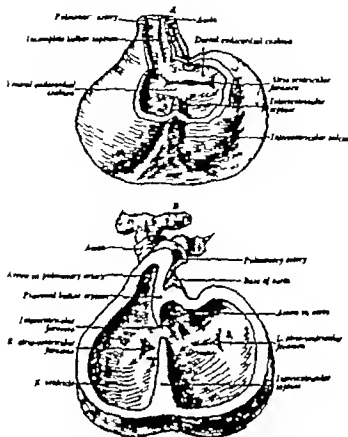


Fig. 3. Schematic ventral views of the opened human heart to show the division of the bulbus and the partitioning of the common ventricle (Kölliker). A, At 5 millimeters, B, at 7.5 millimeters. (From Arry's *Developmental Anatomy*. Courtesy W. B. Saunders Company.)

thin walled endothelial tubes, which soon fuse and develop a dorsal and ventral mesenteric attachment. The ventral mesenteric attachment presently disappears and the heart is left suspended in a pericardial chamber by a temporary dorsal mesocardium which is lost before the heart develops greatly. The endothelial tube forms the endocardium, the splanchnic mesoderm later gives rise to the epicardium and myocardium. This type of heart shows three regions: (1) the atrium which receives blood from the primitive veins; (2) the ventricle; (3) the bulb from which is given off the ventral aorta and the pulmonary artery.

Mammalian and human hearts also develop as two tubular cavities which unite. As the

cardiac tube grows more rapidly than the pericardial cavity in which it lies, it bends to the right, throwing the bulb and the thick walled ventricular limb into a U-shaped loop. A fourth region is now distinguishable, the sinus venosus. The two horns of the sinus venosus soon become very unequal in size, the right side becoming very large and the left very small, due to the shift in flow of venous blood through the liver. This occurs by the time the embryo is 6 weeks old.

The sinus venosus opens into the right dorsal wall of the atrium and then follows a growth of the atrium laterally to the right and the left in two sacculations which are later to become right and left atria.

The bulb and ventricular limbs fuse to one cavity and in the 5 millimeter or 5 weeks old embryo, the heart is composed of three undivided chambers (1) sinus venosus, (2) bilaterally dilated atria, (3) primitive undivided ventricle. The three-chambered heart is developed in adult fishes but in birds and mammals a four-chambered heart is developed in which venous blood circulates on the right side and arterial blood on the left side.

The heart of an embryo of 2 months has attained its general structural characteristics.

There remain four important steps to the formation of the human heart (1) complete division of the atrium and ventricle into right and left sided chambers, (2) the incorporation of the sinus venosus into the walls of the right atrium, (3) the longitudinal division of the bulb and its distal continuation, the truncus arteriosus into the pulmonary artery and aorta, (4) the development of the semilunar and atrioventricular valves.

The second and third changes, as listed, are of interest to us in our particular problem. In embryos of 6 to 8 weeks, the atria increase rapidly in size and the lagging right horn of the sinus venosus is taken up into the wall of the right atrium. By this absorption, the superior vena cava of necessity drains directly into the cephalic wall of the atrium and the inferior vena cava into its caudal wall.

Pulsations in the human heart begin to appear at about the end of the third week, according to Simpkins, the sequence of contraction proceeding from the sinus to the primitive atrium. The first pulsation of the human heart has never been observed, but it probably begins very much as it does in the chicken, in which the initial pulsations occur as little tremors or jerks irregular at first and then settling down to a rhythmical pulsation.

The site of the pace-maker in the embryo heart has remained in the region of the sinus venosus from the time of the first primitive beats and does so as long as the normal heart mechanism persists. The relative position has shifted only in relation to the developing portions of the heart. The sinus or sino-auricular node finally comes to be situated at the junction

of the superior vena cava and the free border of the right auricular appendage and extends down along the sulcus terminalis for a distance of 2 centimeters. The node is 2 millimeters in width and has a special arterial supply, which breaks up into a fine capillary network of nerve cells and fibers forming the excitatory relay from the vagus nerve. Excitatory fibers of the sympathetic are also present.

The mode of spread of the cardiac impulse has been worked out by studies of electrical variation in the beating heart. As the impulse is set up in the sino-auricular node it spreads out uniformly over the walls of both auricles, as when a stone is thrown into a pond and the waves spread concentrically.

The development of the pulmonary artery and aorta continues from the aortic bulb (which includes the truncus arteriosus) in the 5 millimeter embryo from bilateral thickenings which appear in the lumen of the aortic bulb. These thickenings meet and fuse to form two vessels, a dorsally placed aorta and a ventrally placed pulmonary artery. At the same time the interventricular septum is formed so that with a slight clockwise rotation which takes place the pulmonary artery unites with the right ventricle and the aorta unites with the left ventricle.

Since the pulmonary artery and aorta have a common embryological origin from the aortic bulb we find them in a common complete sheath of the visceral layer of the serous pericardium for a short distance, where the visceral layer was attached and made a compensatory growth with the development of the aortic bulb.

When the pericardium is opened from the front it is then found possible to pass the fingers or instruments behind these vessels in front of the atria through what is called the great transverse sinus. This is formed by reason of the reflection of parietal pericardium to envelop the heart.

#### MATERIALS AND METHODS

Three groups of animals were studied in this work. In the first group were 4 dogs each of which was operated upon and a constrictor applied to its pulmonary artery and aorta after the method of Trendelenburg. This was

done to study the reactions of the animals and to observe the effects on the heart, especially its change, contour rate and rhythm, with the constriction by the method of Trendelenburg now used in the operation of pulmonary embolotomy.

In the second group were 3 animals in which a constrictor was applied to the superior vena cava with the view of preserving the respiratory center by maintaining a higher pressure in the capillary bed. This method was soon given up because it seemed to be impractical for either experimental purposes or human application.

In the third and largest group in this series the experimental work was done on 15 normal dogs. In this group the constrictor was applied in such a manner as to obstruct all return venous flow to the heart but no constriction was made of the pulmonary artery or the aorta.

The operative technique used in the preparation of these animals was done under nembutal anesthesia which was given in amounts of 1 cubic centimeter per 7 pounds of weight. Aseptic technique was carried out in only 5 cases, the remainder being done as acute experiments. A three way cannula was placed in the left external jugular vein on each animal and connected to a mercury manometer to study the back pressure developed in the venous system and its relation to the effect on the brain when constriction was applied to the great vessels of the heart.

A three way cannula was inserted in the left femoral artery and hooked to a mercury manometer to study arterial pressures when the great vessels were blocked, and during the recovery periods of the heart after constriction. Sodium citrate solution 10 per cent. was used to prevent coagulation during the experiments. The lesser dilutions would not prevent clotting.

A left parasternal incision was made from the second to the sixth ribs about one-half inch from the midline. The costochondral cartilages were divided close to the sternum and the ribs retracted. The internal mammary vessels were ligated after which the left pleura was incised. All dogs were given artificial respiration of air through a cannula in

the larynx as soon as the pleura was incised. The pericardium was exposed and two stay sutures were placed on the ventral surface 1 centimeter apart and the pericardium was opened widely between them. These sutures were held to maintain a pericardial bed for the heart.

For the dogs in group I, a constrictor of narrow binding tape was used which was easily passed through the great transverse sinus by means of a special sound made in the shape of a large curved needle of No. 6 copper wire. Tightening of this tape made constriction of the pulmonary artery and the aorta.

The same type of constriction was used in the second group as in the first plus a second tape which was placed about the superior vena cava. This caused the opening of the right pleura as it was opened in passing the tape about the superior vena cava with an aneurism needle.

For the third group of cases a special, large double curved sound was made of copper wire which allowed passage of a constrictor through the transverse sinus from right to left, was then passed inferiorly to clear the pulmonary veins and then curved back to be brought out to the right side of the heart over the inferior vena cava. Although with practice this maneuver was easily performed, it seemed subsequently that the tissues could be more gently handled to pass a small rubber tube through the transverse sinus by means of the Trendelenburg sound and then slip the tube over the apex of the heart and gently draw it into place about the junction of the auricle and the inferior vena cava below and through the auricular appendage above. When the constrictor was tightened, it not only occluded the return circulation from the vena cava but also that from the pulmonary veins. It was also easy to pass a new No. 16 male catheter through the transverse sinus with only the right index finger being used as a guide for the catheter. The finger was passed through the sinus from left to right, and the catheter was allowed to follow through from right to left. The catheter was found to be the proper size constrictor for use in our work on dogs.

## RESULTS OF EXPERIMENTS AND OBSERVATIONS

In the following pages are appended the protocols of the animals which were used for the operative and experimental work on this problem

*Dog 1* A white spotted short haired male setter, weighing 38 pounds was used for this experiment. A normal tracing after inserting cannulas showed a rate of 102, with a blood pressure of 50 millimeters' mercury. After the chest was opened under artificial respiration the blood pressure was 56 millimeters and the pulse 162.

During the placing of a constrictor, there was considerable manipulation necessary, with a rise in blood pressure to 77 millimeters with a gradual fall to 61 millimeters over a period of 1 minute and 10 seconds.

When the constrictor was applied, there was an immediate fall in blood pressure to 11 millimeters of mercury and a rise of the venous pressure of 6 millimeters. There followed a gradual drop in arterial pressure during a period of 30 seconds' constriction to 5.5 millimeters and on release of pressure an additional drop to 3.5 millimeters for about 2 seconds. There was no cessation of regular beating but the rapidity of distention of the heart and the force of contraction was surprising. There was especially great distention of the right heart. The corneal reflexes remained normal and the dog had no convulsions. The coronary vessels showed an enormous distention with increased tortuosity.

Following release of constriction, the heart continued with its regular rhythm and with the first full contraction the blood pressure rose from 3.5 to 18 millimeters. With a regular rate of 132, there was a gradual rise in pressure to 70 millimeters. It should be pointed out that this return to normal is much slower than the return of the normal or even of this dog (No. 1A), when constriction was applied to the afferent vessels.

The chest wall was closed in layers, it being impossible to close the pleura. As the last sutures were put in place, the lungs were distended by positive pressure to fill the chest and expel all the air possible. Following closure artificial respiration was stopped and, after 45 seconds, the dog began breathing normally, save for some increased use of the accessory muscles, then it became regular, short and labored. Pulse was 154 but of fair quality. Sheets and heat were applied for a short time, after which the animal was covered and placed in a cage. In the cage the dog appeared to be in mild shock with a pulse of 164 and thready. He reacted from the anesthetic.

On August 5, 1933, he was up in the cage, appeared fairly comfortable, and was friendly. He ate  $\frac{1}{2}$  can of dog-meat with good appetite, and drank some water. His respiratory movements and panting were apparently normal. There was a slight semipurulent discharge from the left eye.

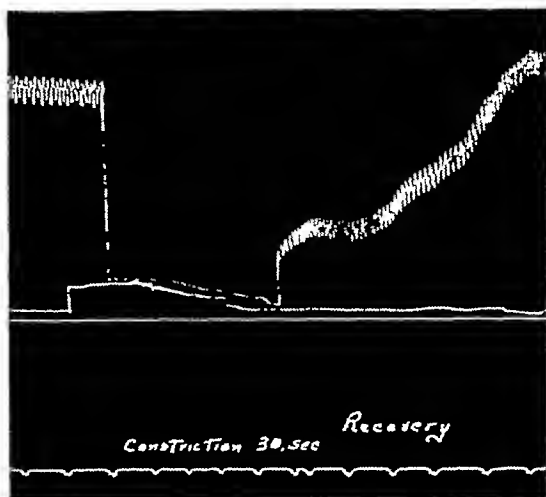


Fig 4. Dog 1. Kymographic tracing showing the slow recovery time of the normal heart when constricted by the Trendelenburg method for only 30 seconds. Compare with Figure 7.

The dog remained well except for a hematoma which formed at the cephalic end of the wound which was drained August 11, 1933, and which continued to drain for about 2 weeks. He lost 6 $\frac{3}{4}$  pounds in weight, weighing 31 $\frac{1}{4}$  pounds on August 14, 1933. This dog was kept and a second operation performed December 13, 1933.

*Dog 5* A brown long haired female dog weighing 34 $\frac{1}{4}$  pounds was used in this experiment. Constriction was applied to the pulmonary artery and aorta, and an ineffectual attempt was made to control the incoming flow of blood to the auricle by digital compression. With application of the constrictor, the heart action became forceful, increased in rate, and with each full powerful beat dilated noticeably. The heart continued with a regular rhythm for 1 minute and 20 seconds, then a few extra systoles appeared. From this time on the force of contraction became weaker with each beat and seemed inversely proportionate to the amount of dilatation. Constriction was held effectively as checked by the manometer for 3 minutes, during the latter part of which the heart was greatly dilated and contractions feeble. Seventy seconds after release of the constrictor, ventricular contractions ceased and the heart distended to its greatest capacity and the musculature remained perfectly flaccid. Five minims of adrenalin (hydrochloride) was given in the right ventricle with no evident effect. One cubic centimeter more of adrenalin was given into the base of the aorta and almost immediately ventricular fibrillation was seen to start in the right ventricle and spread over the whole ventricular musculature. Following a post-mortem examination of this animal, I felt that by digital compression the right auricle could be compressed so as to prevent return flow of blood to the

heart from the vena cava. It seemed obvious that the extreme dilatation with the strain of stretching of the musculature made resection after constriction difficult, if not impossible.

*Dog 6.* A large brown mongrel female weighing 32 pounds was used for this experiment which was conducted with the usual set-up and with constrictor around the pulmonary artery and aorta through the transverse sinus. Digital compression of the right auricle was made with the auricle between the extended index and middle fingers by adduction of the fingers at the same time as the constriction of arteries. The constriction of the pulmonary artery and aorta was held for 1 minute and 40 seconds total time. I was determined to stop constriction short of a lethal time for the dog. With constriction on and compression of the auricle, there seemed to be no less dilatation than without compression. The pupils dilated at 3 seconds and at 1.45 seconds were widely dilated. Corneal reflexes failed at 1.30 seconds. At 38 the animal had one mild convulsion followed by second seizure of about the same type.

The heart was beating with good force in spite of the dilatation after minutes constriction, although the rhythm was some hat irregular. The right heart was more dilated than the left, the line of the later ventricular septum being plainly seen. It was felt that constriction could be safely carried longer. At 2 minutes and 3 seconds, contractions became rapidly weaker and quite irregular with a heart block. At 2 minutes and 40 seconds, the ventricles ceased to contract and as soon as the constrictor was released fibrillation was seen over the right ventricle which spread rapidly to both ventricles.

*Dog 7.* A large mongrel male dog weighing 45 pounds was used for this experiment. The usual set-up of apparatus was used and a constrictor was placed around the pulmonary artery and aorta through the transverse sinus. An attempt was made to put digital compression on the right auricle to prevent the dilatation of the right heart but without evident effect. A normal blood pressure tracing showed the pressure to be 76 millimeters of mercury and after opening the chest and placing the constrictors, the pressure was 35 millimeters. This was a greater fall in pressure than was usually seen. The venous pressure failed to register.

Constriction was held for 3 minutes with the usual dilatation of the heart which usually occurs following the first minute of active beating when constrictor is applied to the great arteries. The arterial pressure made gradual fall to 4 millimeter level in 35 seconds, after which follo ed a period of 3 seconds in which a high pulse pressure was present. The rate during this period was 74 rhythm regular. The heart apparently made normal recovery.

Much to my surprise, while the chest was being closed, the heart was seen to be in state of ventricular fibrillation. This time was estimated to be about 6 minutes after the time of the minute obstruction to circulation.

*Dog 8.* A medium sized black and brown mongrel dog, weighing 38 pounds, was used for this experiment. A normal kymograph tracing showed the blood pressure to be 52 millimeters mercury with a rate of 24. After the chest was opened and the constrictor placed about the pulmonary artery and aorta, second tape was placed about the superior vena cava. This was done by opening the right pleura and passing a threaded dull aneurism needle through the pleura into the posterior mediastinum and bringing one end of the tape out to the left of the superior vena cava. Constriction as then applied to the pulmonary artery, aorta, and superior vena cava simultaneously to stop all circulation for 3 minutes.

The heart was very active for 1 minute, beating widely with full powerful strokes and with what appeared to be an occasional extra systole. The pupils were dilated well at 45 seconds and 1 minute, dilatation was complete. At 1 minute and 2 seconds, the animal staged a mild convulsion followed in succession 0 and 5 seconds apart by four hard seizures. The force necessary to hold the arterial circulation for the first 1 minute was very great, after which the force of the contractions lessened and the heart began to dilate, at first slowly and then as the rate began to slow dilatation became extreme. At 1 minute and 48 seconds, the beating ceased. The venous pressure made gradual rise for 34 minutes during constriction to level of 9 millimeters where it remained until release, except for the rise occasioned by the convulsive seizures. After 3 minutes of constriction, pressure was slowly released and feeble cardiac contractions began immediately—at first one beat every 3 to 4 seconds, then, falling on an irregular rhythm with acceleration of the rate and as increasing force, the heart came to normal size and rate in about 3 seconds. The rate and force with regular rhythm then continued to rise to exceed normal, then gradually slowed to a rate of .04 after 1 minute, no second period.

The pericardium was closed loosely and the chest in layers with no attempt made to close the pleura. Artificial respiration was stopped after the chest was closed and the dog began shallow regular respirations 3 seconds later.

The following day the dog looked well, ate some finely ground meat, and drank little milk. He was up in the cage and friendly. The third day after operation he was listless, hot, and did not drink. The following morning he was dead.

Autopsy showed collapse of both lungs with no air containing them except at the right upper lobe. The pericardium was not distended because it was closed loosely the serous surface was smooth but dull.

*Dog 9.* A long haired black and white mongrel female dog weighing 3 3/4 pounds was used in this experiment. The set up of apparatus and operation was made as has been described and constrictors were placed around the pulmonary artery and aorta and the superior vena cava. A normal pressure tracing showed the arterial pressure was 65 millimeters

before the chest was opened. After the constrictors were in place the pressure was 44 millimeters.

Constriction was applied for 3 minutes. Heart action was strong and regular with some dilatation for 1½ minutes, and then followed marked dilatation, arrhythmia, gradual slowing and loss of force of contraction. The ventricles stopped beating after 25 seconds of constriction from exhaustion in beating against the obstruction, the heart being apparently stretched to its greatest capacity while the auricles continued with a regular rhythm. During constriction, the arterial and venous pressures equalized and after 1½ minutes showed equal levels, according to measurements, varying from 6 to 9 millimeters of pressure.

On release of constriction the ventricles made a few feeble beats for 15 seconds and then stopped. Dilatation was extreme. Cardiac massage was tried without response. Adrenalin 0.5 cubic centimeter was injected into the root of the aorta without effect. One cubic centimeter of adrenalin was then injected into the right ventricle which was followed by a wildly violent response. The manometer was pushed off the drum and blood was forced all the way through the manometer tubing and part of the mercury pushed out of the manometer. The tracing shows a pressure of 105 millimeters but was much higher and the manometer had to be clamped off.

The total time that circulation was suspended, except for the result of cardiac massage, was 5 minutes. After the chest was closed artificial respiration was stopped and normal respirations began at once. Pulse was 142 and of good quality.

The following morning the dog was dead. There was a complete atelectasis of the left lung and nearly complete on the right except for a few air-containing areas in the middle and lower lobes. About 10 cubic centimeters of bloody serous material was present in each pleural cavity. The right heart was widely dilated. No gross changes were present in the brain.

*Dog 4.* A large male police dog weighing 46 pounds was used for this experiment. The set up of apparatus and operation was as has been described with two constrictors placed around the pulmonary artery and aorta and the superior vena cava. The normal blood pressure was 54 millimeters and, after the constrictors were in place, was 42 millimeters. Constriction was simultaneously applied with the two constrictors for 3 minutes. In this instance heart action was at no time entirely discontinued, but after 2 minutes and 10 seconds contractions were feeble although carried on at a regular rhythm. The effect of sudden release of the constrictor was seen here as the heart seemed to lose its rhythm and was overwhelmed for a few beats. The rate and acceleration were slow, but with strong powerful beats the heart action climbed to a rapid rate and a forceful normal rhythm. Pressure returned 40 to 50 millimeters mercury. After the chest was closed respirations began a short time after the tracheal cannula was removed. He was returned to the cage apparently in good condition. The venous pressure showed

a rise to 13 millimeters during the time of constriction.

After operation he looked fairly well for 2 days but apparently had a poor appetite. The morning of the fourth postoperative day the dog was found dead. He had a marked fibrinopurulent pleurisy with a complete left sided atelectasis. The right lung showed atelectasis with partial consolidation of the right lower lobe. The pericardium was distended with a thin purulent fluid with a thick fibrinopurulent exudate on the epicardium.

*Dog 8.* This was a young police dog weighing 30 pounds, and the usual set up of apparatus was made. It had been found by previous experiments on dead dogs that a tube or tape might be passed through the great transverse sinus and then by swinging the sound carrying the tape up to the right side of the apex, the constricting tape would surround the right auricle and the pulmonary veins and thus shut off all return circulation to the heart when tightened and used as a constrictor. In order to obstruct all the vessels, it was necessary to tighten the tape against two or three opposing fingers of the opposite hand.

A sound with a double curve was made of heavy copper wire to carry this constrictor tape. To facilitate the passage of this sound for the first time a suture was placed in the apex of the heart and traction made on the heart to stabilize it and pull it somewhat to the left. The sound was easily passed and the constrictor put in place. A tape was also put around the pulmonary artery and aorta in the usual manner. Constriction was applied to both the pulmonary artery and aorta and the right auricle for 2 minutes. The heart maintained its normal contour and its normal rhythmical contractions during the whole time the tapes were tightened. The dog had no convulsions.

On release of constriction the whole heart, especially the right, filled up rapidly like a balloon and the contractions of the ventricles became feeble and irregular. The heart seemed to be overwhelmed with no ability to recover its normal forceful rhythm. After 4 minutes and 22 seconds the heart went into ventricular fibrillation and the dog expired.

*Dog 9.* This was a large white mongrel dog weighing 45 pounds. The usual set up of apparatus was made and two constrictors were placed as in the previous experiment.

Circulation was obstructed by tightening both constrictors for 2 minutes, after which time the tape about the pulmonary artery and aorta was loosened. It was surprising when no change occurred in the arterial or venous pressures and the contour of the heart, its rate and rhythm remained unchanged, until it was realized that the tape around the auricle prevented all blood flow to the heart. There was no dilatation of the heart. The tape was held on the auricle for an additional 65 seconds. The venous pressure rose to 7 to 8 millimeters and the arterial pressure fell to 7 millimeters during the circulatory obstruction.

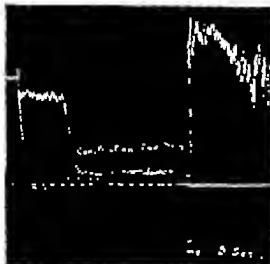


Fig. 5. Dog. Kymographic tracing showing rapid recovery of the normal heart when the aortic valve is constricted. Compare with Figure 4.

When the auricular obstruction to circulation was released, the right heart dilated widely but the regular rhythm supervened and the blood pressure rose in 5 seconds to 85 millimeters. This pressure was maintained for 5 minutes, and then slowly fell to 61 millimeters.

The chest was closed. When artificial respiration was stopped the dog breathed at once. The next morning he was found dead, having succumbed to pneumothorax. The right pleura was intact at post mortem, but a massive atelectasis of both lungs was present.

*Dog 1.* This was a white long haired male mongrel dog which weighed 50 pounds. The usual set-up of apparatus was made and constrictor was placed about the right auricle by use of the special sound.

The circulation was obstructed for 5 minutes. The heart remained normal in size and maintained its normal rhythm for the full time of obstruction. When the tape was loosened the right heart dilated for about 5 seconds but the normal rhythm continued and the heart took up its work immediately rising to 78 millimeters pressure in 6 beats.

The normal blood pressure was 65 millimeters. After the chest was opened and the tape in place, the pressure was 35 millimeters. During circulatory obstruction, the arterial pressure was 7 to 9 millimeters while the venous pressure was of equal height. At 1 minute and 30 seconds the dog had a hard convulsion followed by two somewhat milder seizures 5 seconds apart. During the first convulsion the venous pressure rose to 17 millimeters mercury. It was interesting to note the oscillations of the arterial manometer during constriction of the auricle.

The chest was closed and respirations started 5 minutes and 5 seconds after artificial respiration was

stopped. When returned to the cage, the dog was cold, pulse was 7 and weak, and respirations rapid and shallow. He was wrapped up and heat lamps applied for a short time. The next day he was not active, would not eat or drink. Respirations were rapid and shallow. The following morning he was dead. A bilateral atelectasis was noted—the right lung having a little air containing area in the right upper lobe, the atelectasis being complete on the left side.

*Dog 11.* A large brown long haired male dog weighing 50 pounds was used for this experiment. The usual manometers were hooked up the chest opened, and constrictor passed about the right auricle by means of the special sound. The normal blood pressure level was 65 millimeters of mercury. After the chest was open and the constrictor in place the pressure was 35 millimeters.

Circulation was obstructed for 3 minutes, by tightening the tape around the right auricle. During this time the heart maintained its contour without dilatation and regular forceful contractions of the heart continued. After 1 minute and 35 seconds obstruction the arterial pressure fell from its usual level of 4 millimeters to 1.5 millimeters where it remained until release. The right heart dilated for 30 seconds following release of the right auricle during which time the arterial pressure was 7 to 9 millimeters, but the rate was 100 and the rhythm regular. The force of contraction was too weak to raise the pressure. After this latent period of recovery the pressure started to rise and with a high pulse pressure the pressure gradually rose to 78 millimeters in 60 seconds, the venous pressure showing gradual fall.

After recovery period of 3 minutes, constriction was reapplied for 1 minute during which time the ventricular rhythm was very irregular. The heart did not dilate. The force of contractions of the heart became weak, and the rate rapid so that it was thought advisable to release the pressure. The pressure rose to 59 millimeters almost at once but fell in 15 seconds to 35 millimeters during which time the auricles were in state of flutter and the ventricles were beating wildly with a rate of 160. The apex of the heart seemed to contract normally but the ventricles toward the base seemed to be in a fibrillatory state, which lasted for 1/2 minutes.

Three minute recovery periods were allowed following constriction. Three short periods of obstruction were maintained for 1/2 minutes, 1/4 minutes, and 1 minute. The recovery periods were rapid and the right heart showed only temporary dilatation for a few beats on release of the constrictor. Then followed 5 successive constriction periods of 1/4 minutes each with recovery periods of 3 minutes between obstructions of the circulation. When the constriction was released the regular rhythmic contractions were temporarily slowed by a dilatation of the right heart. The heart made few full strong contractions, the pressure rose rapidly and the rate accelerated, timed at 55 to 60 on several occasions after reaching a stable rate, rhythm, and pressure.



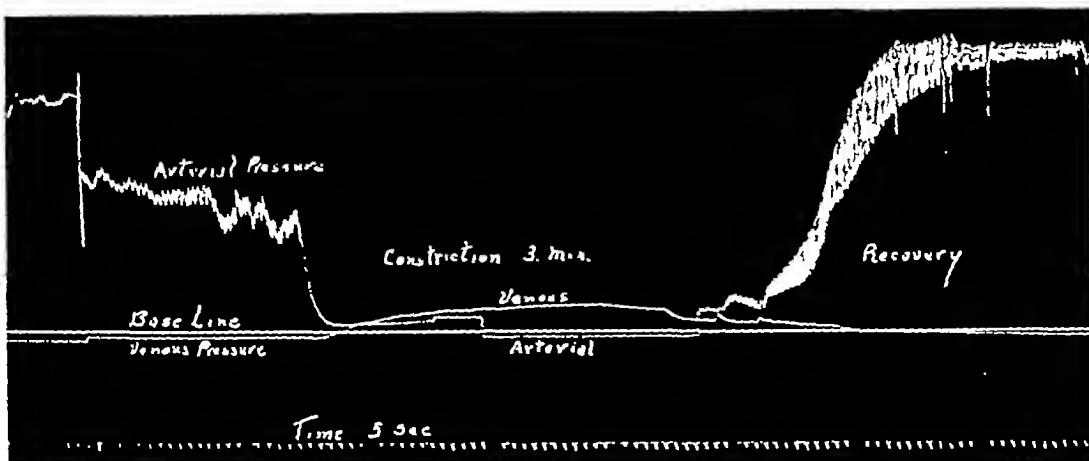


Fig 6 Dog 11 Showing a latent period of recovery of the heart following constriction at the auricle

When obstruction periods totaling 14 minutes were passed, the artificial respirator was disconnected and the dog began to make slow respiratory efforts. This also happened as the experiment terminated.

A total obstruction of the circulation for 21½ minutes was made on this dog at interrupted intervals, the longest of which was 3 minutes and the shortest of which was 1 minute.

**Dog 12** A healthy appearing male police dog weighing 32 pounds was used for this experiment. A complete protocol is given on this dog as being typical of the observations and the work done on this particular group. On the others less detail need be given. The usual set-up of apparatus and exposure was made and a constrictor passed around the right auricle. Some difficulty was experienced in passing the sound because the transverse sinus was smaller than usual, admitting the index finger very snugly. The blood pressure which was normally 61 millimeters of mercury, after the constrictor was in place, was 44 millimeters.

The circulation was obstructed for 2 minutes by tightening the tape about the auricle. The heart continued to beat normally without distention for 1 minute and 40 seconds, and then the right heart began to dilate somewhat and the contractions became slower and weaker.

Physiological Ringer's solution (Locke's formula) (17) had been made up and was freely applied to the heart during the period of obstruction to prevent drying and with a hope of giving an added stimulus to the myocardium. The solution was made up as follows

Sodium chloride  
Calcium chloride  
Potassium chloride  
Sodium bicarbonate

Per cent  
0.9  
0.24  
0.42  
0.02

As soon as the pressure was released without any evidence of temporary fall in pressure the heart took up a forceful beat. In two contractions of the heart the pressure rose from 6 millimeters to 53 millimeters and then continued to rise with a high pulse pressure. In 25 seconds the pressure rose so high that the manometer indicator was forced off the kymograph and with high oscillations went as high as 42 millimeters above the tracing. This made a pressure of 149 millimeters which was higher than any previously seen normally or during the recovery stage. The arterial pressure fell to a pressure level equal to that of the venous pressure which varied from 4 to 7.5 millimeters during constriction, there being a slow rise of 3.5 millimeters after an initial low 35 seconds after the application of the constrictor.

The constrictor was again applied 4½ minutes after release of the first period. This time there occurred an almost identical course with the first except the ventricular contractions which were maintained with a regular forceful rhythm slowed only slightly at 2 minutes and 30 seconds. Obstruction was released at 2 minutes and 30 seconds and in 5 seconds the pressure started to rise from full equal beats. The pressure rose to 116 millimeters and gradually lowered in 3½ minutes to 54 millimeters. Ringer's solution was used less freely.

After a rest period of 5 minutes a third period of obstruction for 3 minutes was maintained. The ventricular contractions were maintained throughout, although they slowed at 2 minutes and 30 seconds and the force seemed somewhat weaker to the hand holding the constrictor from then until release. On release there followed a prompt recovery but this time with a rise in blood pressure to only a normal level of 60 millimeters and a gradual fall to 46 millimeters in 3½ minutes.

A fourth period of constriction was maintained for 4 minutes. At 3½ minutes, the ventricles were beat-

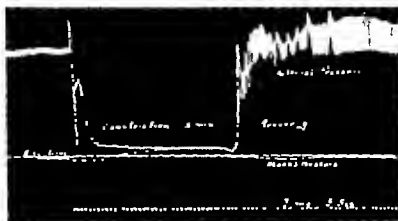


Fig. 7. Dog 1A. Kymographic tracing showing arterial and venous pressures with constriction of afferent heart catheter for 3 minutes and the prompt recovery which follows. (Compare with Figure 4 made from same animal 4 months previously showing slow recovery when efferent catheter was constricted for only 30 seconds.)

ing slowly but contractions were strong, regular, and complete. The rate had obviously slowed. There was no distention. The dog staged one hard convulsion at 3 minutes and 4 seconds and his pupils were widely dilated with absent corneal reflexes. At 5 minutes and 43 seconds the right heart began to dilate and contractions weakened although no evident change was made in the manner of constriction. When the tape was released the right auricle and ventricle were well distended but dilated widely on release. The heart began weak, very irregular beats without force and with no rise in blood pressure. After 35 seconds of these irregular feeble beats the ventricles began to fibrillate. Ringer's solution was freely applied during these periods.

This dog survived 7½ minutes of circulatory obstruction but not an additional 4 minute period.

**Dog 13.** A large, thin male police dog weighing 37 pounds was used. This dog had a rapid heart rate of 52. His irregular respirations before operation. The usual set-up and exposure was made with constrictor tape applied to the right auricle. The artificial respirator, as not working properly during manipulation in passing the sound and the animal developed a marked cyanosis and a 3 heart block lasting 45 or 50 seconds. Soon after the respirator was fixed and the heart was auscultated with Ringer solution, the rate picked up and the rhythm became regular.

Obstruction of the right auricle was held for minutes. The heart remained regular without distention but the venous pressure rose 3 millimeters higher during compression than the arterial pressure. At 1 minute and 55 seconds the dog had one hard convulsion and following release the heart recovered promptly the pressure rising to a high level of 93 millimeters. During 5 minute rest period, the pressures fell to 38 millimeters.

Constriction was applied for 3 minutes. At 2 minutes and 0 seconds of constriction the heart beat became slow and irregular. The application of Ringer's solution was decided stimulus to the heart, the rate increased to about normal and the rhythm again became regular. At 1 minute and 20 seconds the dog had a convulsion followed by another 3 seconds later.

Following release of the circulation, the heart took up a feeble regular rhythm with blood pressure of 15 millimeters which lasted for 30 seconds without signs of recovery. Ringer's solution was applied freely and the heart immediately began more vigorous efforts, showing gradual rise in blood pressure to 45 millimeters in 50 seconds. The continued application of Ringer's solution made the beat tumultuous although there was no greater rise in blood pressure. The rhythm returned to normal but no more solution as applied. The stimulation of this solution for the heart was demonstrated no the heart on three different occasions, during the course of this experiment.

A third period of constriction of minutes and 43 seconds was followed by weak irregular contractions for 35 seconds, during which time the right heart was greatly dilated and after which the ventricles began to fibrillate while the auricles maintained regular rhythmic beating.

**Dog 14.** This dog was brown and black white spotted male dog of the setter type which had previously been operated upon August 4, 1933, and the pulmonary artery and aorta clamped off for 50 seconds. The usual arterial and venous manometers were used and the chest was opened by left parasternal incision from the second to sixth ribs. When the pleura was opened no adhesions were encountered. The right medial pleura was slightly thickened. The pericardium and epicardium were free and their sur-

faces shiny, with 2 to 3 cubic centimeters of serous fluid present in the pericardial sac. The former line of incision in the pericardium was covered by a thin layer of fat. The only adhesions present were in the great transverse sinus. Here the adhesions were firm and fibrous and some difficulty was encountered before these were broken and it was possible to pass a sound through the sinus. A tape constrictor was then placed about the right auricle and tightened for 3 minutes. The heart action remained strong and regular at the rate of 104 until 2 minutes and 45 seconds, when the rhythm became somewhat irregular. A prompt recovery followed with the heart beating regularly and its action strong. No convulsions appeared.

After 5 minutes, a second constriction period was held for 2 minutes. Heart action weakened at 1 minute and 28 seconds and became irregular at 1 minute and 40 seconds. The heart was not dilated and when released dilatation of the right heart occurred for a few beats but was overcome by a prompt recovery. His pulse following constriction was 152. Three interrupted sutures were placed in the pericardium and the chest wall was closed in layers. He was placed under lamps to warm him and then covered when put into the cage.

The following day he was out of the cage and around with the diener and seemed active and in no distress.

December 16, 1933, dog was active, respirations good and deep—rate 22 and pulse 112. There was a dependent edema and redness of the wound at the upper end, extending into the neck.

December 21, 1933, small abscess was draining at upper angle of wound. The dog was in good condition and active.

December 26, 1933, animal was not eating or drinking well, wound closing nicely.

December 30, 1933, dog was found dead in cage and was thrown out before autopsy could be done.

*Dog 14.* A small male wolf dog weighing 28 pounds was used. The usual set-up of apparatus was used and a constrictor placed about the right auricle. Constriction was applied for 2½ minutes. At 2 minutes and 15 seconds contractions became irregular and rate slowed. At 2 minutes and 30 seconds, there was marked weakness of contractions and irregularity so that it seemed necessary to release the obstruction. Release was followed by feeble, irregular contractions which failed to raise the blood pressure. After 1 minute 0.5 cubic centimeter of adrenalin was injected into each of the right and left ventricles. A most marked response followed. The rate became very rapid and pressure rose to 168 millimeters of mercury. One convulsion followed 30 seconds after release of the constrictor.

A second constriction period of 2 minutes was maintained without event. The heart did not dilate. After 3 minutes' rest as the tape was tightened for a third period, the ventricles began beating wildly in a ventricular fluttering state. The tension was varied without change. After about 10 seconds the con-

striction was loosened and my fingers opposing the constrictor were changed, then the tape was immediately tightened, a normal rhythm followed.

In all eight periods, constriction was maintained in which all circulation was blocked for times of 2, 2½, 3, and 4 minutes. The time and order in which these periods came were

Period	1	2	3	4	5	6	7	8	9	Totals	9
Time	2½	2	3	2	2	3	3	4	3	death	1½

After the fourth period of constriction, which was at the end of 9½ minutes of interrupted obstruction to the circulation, the artificial respirator was disconnected and 48 seconds later the dog began to make respiratory efforts. After the sixth period, contractions were weak and the heart dilated as soon as obstruction was released. After 30 seconds of feeble contractions 5 cubic centimeters of adrenalin was injected, one-half into each ventricle with immediate response but less active than with the first adrenalin given.

In all, the heart survived 31½ minutes of periodic obstruction. Following the ninth period of 3 minutes the heart showed a 2 r heart block which was maintained for 3 minutes and followed by ventricle fibrillation.

*Dog 15.* A large male Russian wolfhound weighing 42 pounds was used for this work. The usual set-up was used and a constrictor placed around the right auricle and tightened for 3 minutes. The rhythm remained regular throughout. The heart remained normal in size and made a very prompt recovery on release of pressure. The normal blood pressure was 75 millimeters and when constrictors were in place was 55 millimeters. Following release the pressure rose to 114 millimeters, then gradually lowered to 51 millimeters. Ringer's solution was applied freely during this period of obstruction. The high pressure may well be due in part to this, for it was not used to more than moisten the heart in the next period. A 5 minute recovery period was allowed between periods.

A second period of constriction was applied for 4 minutes and a kymographic tracing was taken of this period. Except for a slight slowing of the rate after 3 minutes and 10 seconds nothing remarkable occurred. No convulsions appeared and a prompt recovery followed. Ringer's solution was applied to the heart to moisten exposed surfaces.

A third period of obstruction was applied for 4½ minutes. At 3 minutes there was a decided slowing and weakness of the heart beat. Ringer's solution was applied freely and the rate and force returned even stronger than the normal immediately following the application. The rate slowed slightly and the force of contraction became weak, remaining regular, but when the constrictor was released the recovery was prompt.

In the fourth and last period the circulation was obstructed for 5 minutes. Again a stimulus was seen from Ringer's solution when applied to a somewhat irregular and rapidly weakening heart after 2 min-



Fig. 3 Dog 7. Kymographic tracing showing the effects of constriction of the afferent heart vessels for 6 minutes, followed by latent period of recovery of 30 seconds in which the heart beat regularly but weakly. Recovery followed an injection of 3 millimeters of adrenalin hydrochloride into each ventricle.

utes and 35 seconds. During the last 38 seconds the right heart dilated and the rate and rhythm became irregular again, while during the last 8 to 10 seconds the rate was very slow. Convulsions occurred at minutes and 45 seconds and at 4 minutes. Recovery was prompt, and the experiment terminated. The circulation in this case was completely obstructed for periods of 3, 4, 4½, 5 minutes with 3 minute rest periods between, making a total time of 6½ minutes. When the artificial respirator was disconnected as the experiment was terminated, the dog made vigorous respiratory efforts for 3 minutes, 40 seconds, and at 5 minutes, 8 seconds 10 hard convulsions occurred.

Dog 16. A large pointer dog weighing 45 pounds was used for this experiment, and the cannulas were inserted in the vein and artery. Constriction was applied to the auricle for 3½ minutes. At the end of 3 minutes the rate had slowed from 121 to 63 and the contractions were very weak. When the tape was released, prompt recovery followed. Ringer's solution was freely applied and the pressure rose to a height of 125 millimeters. Five minute rest periods were allowed.

Obstruction to the auricle was again maintained for 4½ minutes. Contractions were strong and regular for 3½ minutes, then gradually weakened and slowed but remained regular. Because of the weakness of contractions, constriction was released. Recovery was prompt. Ringer's solution only was used freely as stimulant. Respiratory efforts were noted throughout this period and one convulsion occurred as the constrictor was released.

Constriction was again applied for 4 minutes. The contractions soon weakened and these were stronger when Ringer's solution was applied. The rate again slowed and contraction weakened. At 3 minutes

and 30 seconds a 12 heart block was noted. At 3 minutes and 35 seconds 3 heart block was present and at 3 minutes and 55 seconds the heart stopped.

Release of constriction caused marked dilatation of the right heart and only irregular slow contractions of the heart occurred. After 30 seconds adrenalin hydrochloride, 3 millimeters, was given into each ventricle. Ventricular fibrillation followed immediately after the adrenalin injection. The animal survived constriction of 6½ minutes of obstruction to the circulation held in two periods, but failed to survive another 4 minute period.

Dog 17. A brown mongrel male dog weighing 36 pounds was used for this experiment. The usual set up was made and a constrictor placed about the right auricle. The constrictor was tightened and obstruction maintained for 6 minutes. The normal blood pressure was 9 millimeters and after the chest was opened and the constrictor in place, as 43 millimeters. With constriction, the arterial blood pressure fell to 7.5 millimeters and the venous pressure to 6 millimeters.

The heart rate was 8 during constriction and maintained regular rhythm and normal size until the last half minute when the rate slowed and contractions weakened somewhat. Following release the heart beat feebly and showed no sign of recovery. After 30 seconds, adrenalin hydrochloride 3 millimeters was injected into each ventricle and an immediate recovery followed. The blood pressure rose to 97 millimeters and remained at 80 millimeters for at least 5 minutes. One convulsion occurred at minutes and second hard seizure followed at 3 minutes and 35 seconds.

A second constriction period of 3 minutes was uneventful. For the third period of constriction, obstruction was maintained for 4 minutes. After 3 min-

utes and 10 seconds a 2:1 heart block occurred. When constriction was applied for the fourth period, the rhythm became so irregular it seemed wise to let the constrictor loose and reapply it. Obstruction was held 10 seconds then released, the fingers and constrictor changed in position, and then tightened and held for 4 minutes. At 3 minutes and 20 seconds, the rate was 46. The rate continued to slow but on release the heart recovered promptly. A 3½ minute constriction period was held. The rate slowed gradually after 2 minutes and 55 seconds, being entirely stopped for the last 5 seconds. A prompt recovery followed.

Then followed a series of six 4 minute periods of obstruction to circulation except the ninth period was carried 4½ minutes. During the eighth period the rate slowed to 15 beats per minute.

After the last period the heart dilated and showed no sign of progress to recovery. After 2 minutes and 12 seconds 3 millimeters of adrenalin was given in each ventricle and the heart recovered a regular rhythm. The experiment was terminated voluntarily.

Period Time	1	2	3	4	5	6	7	8	9	10	11	Total
	6	3'	4'	4'	10"	3½'	4	4	4	4½'	4	4
												Total 45"

*Dog 18* A large police dog weighing 42 pounds was used for this experiment. The usual set-up was made and a constricting tape passed around the right auricle and held for 3½ minutes. The heart maintained a regular normal rate, did not dilate and on release took up its work without missing a beat. The right heart dilated moderately for a few beats immediately following release of constriction. A 5 minute rest period was allowed.

Constriction was again applied for 4 minutes. During the last 30 seconds, the right heart dilated widely without missing a beat. The right heart dilated moderately for a few beats immediately following release of constriction. A 5 minute rest period was allowed.

Constriction was again applied for 4 minutes. During the last 30 seconds the right heart dilated widely without change of pressure relations on the drum. On release of the constricting tape the heart dilated, made a few feeble contractions and started a ventricular fibrillation.

*Dog 19* A large old police dog weighing 52 pounds was used for this experiment. The usual set-up was made and a constricting tape passed about the right auricle. The coronary vessels were thickened and tortuous in appearance.

Constriction was applied for 5 minutes. The heart action remained strong for 4½ minutes, although at 3 minutes and 12 seconds, the rate halved and a 2:1 block was noted. Contractions were strong and regular. At 4 minutes and 40 seconds the 2:1 block disappeared, the rate doubled, but the heart action was very weak. At 4 minutes and 45 seconds, the right heart dilated. At 4 minutes and 52 seconds, the ventricular action was stopped, the heart dilated

and stopped in diastole. On release the heart distended widely and very weak irregular purposeless movements were seen. One-half cubic centimeter of ephedrin was injected into each ventricle and the heart immediately set up a ventricular fibrillation.

*Dog 20* A large white mongrel female dog weighing 42 pounds was operated upon with the usual set-up of apparatus made and a constrictor placed about the right auricle. Constriction was applied for six 2 minute periods, which seemed to be long as this heart would go without dilatation with an onset of irregular rhythm and marked weakening of the force of contractions.

For each period it was thought that the time of constriction could be prolonged. Prompt recovery always followed. For the seventh period the constriction was carried for 3 minutes, in spite of dilatation and weakening. A prompt recovery followed. The next obstruction period was carried for 4 minutes, the last 20 seconds of which the heart dilated and ventricular contraction ceased. On release of the tape the heart greatly distended, the ventricles made slow feeble beats but after 30 seconds made no sign of recovery. One-half cubic centimeter of ephedrin in each ventricle was given and ventricular fibrillation immediately followed.

*Dog 21* A small white male dog weighing 24 pounds, anesthetized with ether instead of nembutal, was used for this experiment. A No. 14 catheter was passed through the transverse sinus and then swung around the apex of the heart to act as a constrictor of the auricle. This heart did not tolerate constriction well and was carried for only 1½ minutes. At 1 minute and 15 seconds the heart dilated, rhythm slowed markedly and at 1 minute and 27 seconds the heart stopped beating. Prompt recovery followed, although the rhythm was somewhat irregular for 1 minute. After 3 minutes constriction was applied for 2 minutes with similar results. A 5 minute recovery period was allowed.

Constriction was applied for 3½ minutes. The last 15 seconds the heart made only a few feeble beats and was widely dilated. On release the dilatation became extreme and the heart beat with weak flaccid strokes, was irregular for an additional 2 minutes. During this period the dog made irregular respiratory efforts, the effects of which made sharp rises in venous pressure. No massage or manipulation was made. When no sign of active recovery was seen, adrenalin hydrochloride 0.5 cubic centimeter was injected into each ventricle and a prompt recovery followed. The pressure rose to 94 millimeters between 1 minute and 45 seconds a 2:1 heart block was present.

With light ether anesthetic, the pupillary reflex was retained. On constriction the pupil contracted so at 30 seconds the pupils were pinpoint and then the pupils dilated so at the end of 1 minute they were widely dilated and remained so until release and recovery.

Two 3 minute constriction periods followed. The heart dilated each time before release, but recovered

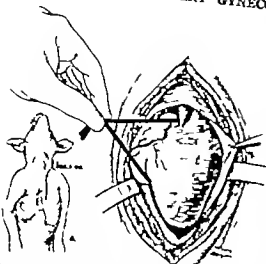


Fig. 9. Drawing showing the constrictor in place about the afferent vessels of the heart. When the circulation is obstructed normal cardiac contractions continue and the heart remains normal in size.

rather promptly after short periods of irregularity. The experiment was terminated.

#### DISCUSSION OF OBSERVATIONS

As referred to under "The Problem" the motive for undertaking this work was to see if a more efficacious method of constriction of the great vessels of the heart might not be determined. In answer to this question it seems that the most important conclusion drawn from this experimental study is that it is possible to constrict the great vessels of the heart by a more satisfactory method than by any now in use.

This constrictor is so placed that all blood returning to the heart is cut off and this factor in itself provides many advantages. As was pointed out some of the most obvious difficulties occurring when the pulmonary artery and aorta are obstructed are caused by the great distention occurring in the heart. The heart exhausts itself rapidly laboring to overcome an impassable obstruction. In 3 dogs the pulmonary artery and aorta were constricted one for the short period of 30 seconds and the 2 others for relatively short periods of 3 minutes and 40 seconds, and 3 minutes. In the latter 2 the dogs failed to survive and it seems logical to believe that

some after-effect of distention is responsible for the failure of these hearts to recuperate.

The difference in the manner of recovery of the normal heart when these two methods of constriction are applied is certainly well illustrated on Dog 1 which was used for constriction by the older method, then 4 months later constricted by the new method, and reported under Dog 1A.

When the pulmonary artery and aorta were constricted for only 30 seconds the heart made a steady slow recovery over a period of 35 seconds, making 70 beats while following 3 minutes constriction of the auricle, the same heart made a similar recovery in about 13 contractions and in 10 seconds.

In Dog 10 following constriction of the auricle for 3 minutes, the blood pressure reached a level high above normal in 9 contractions and 5 seconds. Compare Figures 4, 5 and 7.

There are apparently many factors which are combined to determine the final result of obstruction of these great vessels, but the most likely causes of cardiac damage are apparently two (1) exhaustion of the myocardium and (2) interference with the normal cardiac impulses and rhythm.

The death of 2 dogs of 3 used may have been only incidental for it is too small a group from which to draw conclusions. However as demonstrated by the experimental work of Laeven and Slevens which was performed on rabbits it would seem that death was the rule for constrictions longer than 3½ minutes, and only a few animals survived for longer periods. These 2 animals followed the rule.

These dogs quickly developed signs of interference or interruption of impulses from the pace-maker. This may be due to any one of a number of causes or to a combination of these several effects. It is possibly from the muscular fatigue occasioned by the excess work put onto the heart at the time of obstruction. Lewis has demonstrated that

Heart block may be induced readily in cats, less readily in dogs by asphyxiating them. Such block is independent of the vagus occurring equally after fall saturation with atropin or section of the vagi. It is also independent of blood pressure changes, of dilata-

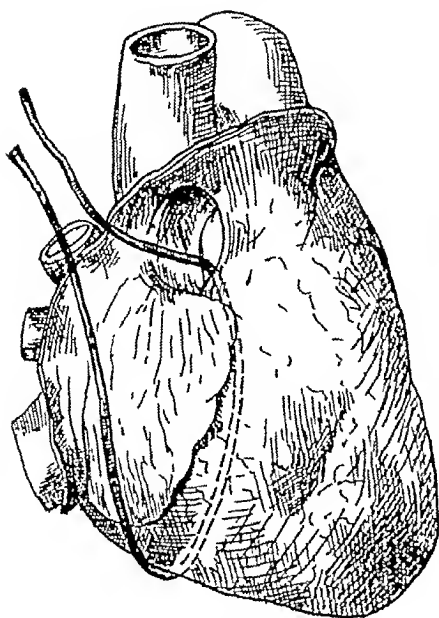


Fig 10. The heart viewed from the right and in front, showing the constrictor in place about the afferent vessels through the great transverse sinus and as it crosses the right auricle

tion of the heart, and of excessive accumulation of carbon dioxide in the blood, it probably results from lack of oxygen and is perhaps due to an excess of acid products in the muscle

That anoxemia plays a part in the development of cardiac arrhythmias or heart block, there seems little doubt and the excess work occasioned by obstruction of the pulmonary artery and aorta may be a factor in the production of anoxemia more quickly than when the afferent vessels of the heart are shut off and the heart has relatively no work to carry on. Certainly anoxemia promotes early muscular fatigue and excess work produces early anoxemia, so that a vicious cycle is set up.

The intracardiac pressure relations are difficult to evaluate in regard to their effect on the heart. This much may be safely stated, that when there is obstruction of the efferent vessels with a high intracardiac pressure arrhythmias appear in some dogs as early as 1 minute (Dog 2) and most of the hearts became irregular as early as 1 minute and 30 seconds after constriction, while with obstruc-

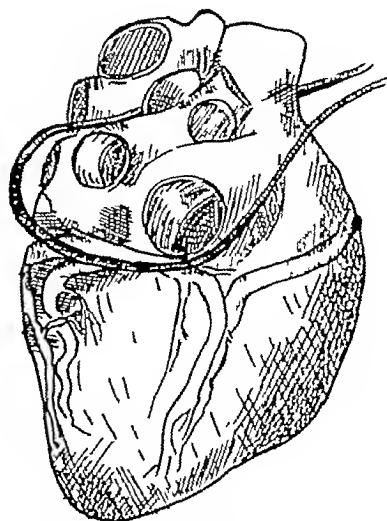


Fig 11 Drawing of the heart viewed from below showing the constrictor in place about the afferent vessels as it passes through the great transverse sinus, under the two branches of the pulmonary artery, to go around the pulmonary veins and the inferior vena cava

tion of the afferent vessels and no increase in intracardiac tension irregularities do not usually appear until 2 minutes and 15 seconds, and many go 3 minutes, and one heart, Dog 17, went 5½ minutes with a regular rhythm during constriction. In general the maintenance of a regular cardiac rhythm during constriction seemed to be a fair index as to the length of time the obstruction could be maintained and have the animal recover.

We have thus outlined some of the advantages of obstructing the great heart vessels on the venous side, rather than on the arterial side. Because the heart may beat freely and not be overdistended and quickly exhausted, it is possible to interrupt circulation for longer periods than when constriction is applied to the pulmonary artery and aorta.

In all instances except on 3 dogs of 15 used, circulation was obstructed for periods of 3 minutes or longer with survival of the animals. These three exceptions are: Dog 19 was obstructed for 5 minutes and failed to survive, Dog 10 was obstructed for only 2 minutes and not constricted more after surviving, Dog 8 succumbed after 2 minutes' constriction. This was the first dog in which this method was

## SURGERY GYNECOLOGY AND OBSTETRICS

tried in many instances it is difficult to tell just how long the constriction might be carried and still have the dog survive for they recovered several times when the obstruction was carried beyond what was considered a safe time. It seems reasonable to say how ever that the time of obstruction to the circulation by this method may be safely carried in the normal dog for a period of  $3\frac{1}{2}$  minutes. Although in all instances except those mentioned constriction was carried beyond this time and in one instance was held as long as 6 minutes, this time of  $3\frac{1}{2}$  minutes seems to be the upper limit of safety.

The freedom from distention of the heart which this method allows and the continuation of the normal rhythm gives the advantage of a more rapid recovery of circulation even with longer periods of interruption of the circulation. When the constrictor is released there is a temporary dilatation of the right heart which is usually overcome in only a few heart beats and even during this time arterial circulation is going on so that in these few heart beats the blood pressure reaches a normal level.

That there is a possibility of interference with the pace maker when the constrictor is applied about the right auricle must be recognized so that when it is seen it may at once be relieved by a change of position of the constricting tube or tape. This phenomena was encountered in two instances in which a ventricular flutter came on with the application of the constrictor. Release and change of position in both instances corrected this condition and a normal rhythm followed. In Dog 11 this was seen with the second constriction period when the rhythm was very irregular and rapid and when released because the heart was weakening so rapidly the heart beat at a rate of 220 for  $3\frac{1}{2}$  minutes before it recovered. Again, in Dog 14, at the beginning of the third constriction period the condition was seen and a change of position altered the condition.

When the heart is exposed to air and warmth, the drying action which occurs on the surface seems very rapid. It was necessary to apply some solution to keep the heart moist. The 2 solutions which were tried were

physiological saline and Ringer's solution. Physiological salt solution was used first and seemed to have no effect other than merely to keep the heart moist. When warm Ringer's solution was applied to its surface it was delightful to see in several instances a very marked stimulus to the heart. Although the sustaining qualities of Ringer's solution on the heart of the frog has been recognized for many years, it has not been mentioned in works dealing with cardiac surgery. It seems well at this time to call attention to the beneficial effects to be derived from the use of Ringer's or Locke's solutions when applied to the heart. Ephedrin solution was used in two instances and both times caused immediate ventricular fibrillation (Dogs 19 and 20). Both instances were after prolonged and repeated constriction respectively.

No dogmatic statements can be made in the conclusion as to the effects on the brain and vital medullary centers when the afferent vessels of the heart are constricted by this method. It seems from the evidence presented by these animals in both the group which were kept alive following constriction and those done as acute experiments, that no serious damages to these vital centers could be demonstrated except following repeated, prolonged obstruction of the circulation.

In the animals which were kept alive in which either the superior vena cava or the auricle was constricted there was no delay in the return of respiration in any dog and the following day the dogs seemed well oriented, friendly and well. The cause of death seemed in no way related to the brain or vital centers, but to lung conditions. That dogs are not well suited to experimental work which involves opening of the pleural cavity has been demonstrated by Graham who has shown the presence of open interpleural sinuses in the mediastinal pleura. This means that one pleural cavity in the dog may not be invaded without the development of a bilateral pneumothorax which is not tolerated.

It was possible to demonstrate clearly in 3 dogs in which it was tried that the respiratory center remained in a functional state after prolonged constriction. This could be



done for only brief intervals, nevertheless seemed satisfactory when by disconnecting the artificial respirator the dogs would soon make definite respiratory efforts. In Dog 11 this occurred after 14 minutes and after 21½ minutes of interrupted constriction, in Dogs 14 and 15 after 9½ minutes and 16½ minutes of interrupted constriction, respectively. In the other dogs this was not tried. That the vital centers will withstand such prolonged periods of obstructed circulation, some of the interrupted periods being 4 and 5 minutes of continuously blocked circulation, seems to support the contention that in this method of constriction the vital centers are protected by promoting a stasis of venous blood in the capillary bed from back pressure. It would be a problem of interest in itself to investigate the changes which occur in the brain when the various types of constriction are applied for interruption of the circulation. This might be done by direct observation by placing a window in the skull to observe the vascular changes which occur and by measuring the pressure changes which take place within the skull.

This method of constriction of the great vessels of the heart presents advantages which have heretofore not been available for human application. It only remains necessary to apply this technique which seems reasonable and entirely possible.

#### SUMMARY

1. A new method of constriction of the great vessels of the heart is described whereby the obstruction is placed on the afferent rather than on the efferent side of the heart.

2. It would seem that the constriction near the venæ cavæ lessens the likelihood of respiratory failure.

3. The time of constriction may be safely prolonged to 2½ minutes in the normal dog.

4. This method of constriction protects the normal cardiac conduction mechanism from the damages of cardiac distention.

I wish to express my sincere appreciation to Dr. Raymond W. McNealy, surgeon in chief of Wesley Memorial Hospital in Chicago, for his helpful suggestions and assistance in carrying on this work, and to Dr. Eugene Birchwood, who assisted in the experimental work in this problem.

#### BIBLIOGRAPHY

1. AREY, LESLIE BRAINERD. *Developmental Anatomy*, p. 261. Philadelphia and London W. B. Saunders Co., 1930.
2. BOWDITCH, H. P. Quoted by Howell, *Textbook of Physiology*, p. 583, loc. cit.
3. CHURCH, HENRY M. Thrombosis of the pulmonary arteries with reference to treatment by inhalation of oxygen. *Tr. Edinburgh Obst. Soc.*, 1892, 17: 2-213.
4. CRAWFORD. Quoted by Nyström, loc. cit.
5. CUTLER, ELLIOTT C. Pulmonary embolectomy. *New England M. J.*, 1933, 209: 1265.
6. EICHELTER, G. Die Operation der Lungenembolie nach Trendelenburg. Bericht ueber die bisher bekannt gewordenen und acht weitere Faelle. *Chirurg*, 1932, 4: 209.
7. GASKELL, W. H. Quoted by Howell, *Textbook of Physiology*, p. 597, loc. cit.
8. GRAHAM, E. A. Quoted by Cutler, Elliott C., and Beck, Claude S. *Surgery of the Heart and Pericardium*. Nelson's Loose Leaf Living Surgery, vol. 4, 259. New York: Thomas Nelson & Sons, 1932.
9. GRISWOLD, RETTIG A. Trendelenburg operation for pulmonary embolism. *Ann. Surg.*, 1933, 98: 33.
10. HOWELL, W. H. *Textbook of Physiology*, p. 679. Philadelphia and London W. B. Saunders Co., 1926.
11. KIRSCHNER, M. Ein durch die Trendelenburg'schen Operation geheilter Fall von Embolie der Arteriae pulmonalis. *Arch. f. Klin. Chir.*, 1924, 133: 312.
12. Idem. Quoted by Nyström, loc. cit.
13. KRUEGER. Ein nach Trendelenburg operierter von Embolie der Lungenarterie. *Zentralbl. f. Chir.*, 1909, 21: 757.
14. LAEWEN, A., and SIEVERS, R. Experimental Untersuchungen ueber die chirurgisch wichtigen Abh ngen der grossen Gef sse in der Nahe des Herzens unter besonderer Beruecksichtigung der Verhaeltnisse bei der Lungenembolie-Operation nach Trendelenburg. *Deutsche Ztschr. f. Chir.*, 1903, 94: 580.
15. LEWIS, SIR THOMAS. *The Mechanism and Graphic Registration of the Heart Beat*, p. 169. London: Shaw & Sons, Ltd., 1925.
16. LUNDY, C. J., and WOODRUFF, L. W. Experimental heart block. *Arch. Int. Med.*, 1929, 43: 184.
17. MACLEOD, J. J. R. *Physiology and Biochemistry in Modern Medicine*. St. Louis: C. V. Mosby Co., 1926.
18. MAKINS, SIR GEORGE H. *Gunshot Injuries of the Blood Vessels*. New York: W. Wood & Co., 1910.
19. MCNEALY, R. W. The place of elective vein ligation in blood-vessel surgery. *Surg., Gynec. & Obst.*, 1925, 40: 45.
20. MEDAUGH, F. W. *Elementary Hydraulics*. New York: D. Van Nostrand, 1924.
21. MEYER, A. W. The operative treatment of embolism of the lungs. *Surg., Gynec. & Obst.*, 1930, 50: 891.
22. Idem. Eine weitere (meine vierte) erfolgreiche Lungenembolie-Operation. *Deutsche Ztschr. f. Chir.*, 1931, 231: 586.
23. Idem. Eine weitere (meine vierte) erfolgreiche Lungenembolie-Operation. *Emanuel Libman Anniversary volumes*, 1932, 2: 815.
24. NURNBERGER, L. Ueber die Zunahme der Thrombosen und Embolien. *Med. Klin.*, 1930, 26: 576.
25. NYSTR M, GUNNAR. Experiences with the Trendelenburg operation for pulmonary embolism. *Tr. Am. Surg. Ass.*, 1930, 43: 18.
26. OPPEL, W. A. Wiegung operation und der reduzierte Blutkreislauf (Hbs.). *Zentralbl. f. Chir.*, 1913, 40: 1241.

## SURGERY GYNECOLOGY AND OBSTETRICS

- 27 RAVEI Quoted by Nyström, loc. cit.
- 28 SAUERFELDER, F Quoted by Eschschter loc. cit. p. 309
29. SCHUMMEGER, W Ueber die nach 18779 Operationen  
beachteten Lungenembolien Schwanz med.  
Wchnschkr 1908, 58 78
30. SCHUMMEGER, E D Beitrag zur Trendelenburg'schen  
Operation bei Lungenembolie Bern z. klin. Chir  
9 4, 90 188
31. SEVERIN, R Ein Fall von Embolie der Lungenarterie  
nach der Methode von Trendelenburg operiert.  
Deutsche Ztschr f Chir 1908, 98 26
32. SHUMKIN, C S Textbook of Human Embryology  
p 267 Philadelphia F A Davis Co 08
33. SELL, ALBERT M The relation of obesity to fatal  
postoperative pulmonary embolism Arch. Surg  
1917 5 37
34. TRENDLENBURG, FRIEDRICH Zur Hirschsprung  
Zentralbl f Chir 1907 34 301
35. Idem Ueber die operative Behandlung der Embolie  
der Lungenarterie Verhandl d deutsch Gesellsch  
f Chir 1908, 37 ( ) 89
36. Idem. Zur Operation der Embolie der Lungenarterie  
Deutsche Med Wchnschkr 1908, 34 7
37. V. KILB, M Quoted by McNealy loc. cit.
38. VAN SWETEN, G Quoted by Church loc. cit.
39. VINCOW, RICHARD I Ueber die Verstopfung der  
Lungenarterie II Weitere Untersuchungen ueber  
die Verstopfung der Lungenarterie und ihre Folgen.  
Abd. In Rudolf Virchow—Thrombose und Em-  
bolie, 1846—895 By Rudolf Virchow—Leipzig, 10 o.  
(Compiled by Besche but Vincow's previous pub-  
lication)

## A RELIABLE METHOD FOR TESTING THE STERILITY OF SURGICAL CATGUT SUTURES

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THE object to be achieved in conducting bacteriological examinations of most substances is the demonstration of the presence or absence of some particular species of bacteria. However the purpose of the bacteriological tests applied to surgical catgut sutures is quite different, for in this case the presence of any and all forms of bacteria is being sought. Such a procedure necessarily must involve a highly specialized technique carried out under the most rigid conditions and must embrace a search for the spores and vegetative forms of all anaerobic as well as aerobic bacteria.

## THE NEED FOR A RELIABLE TEST

After making extensive bacteriological tests over a period of years of catgut sutures manufactured in various countries, several experienced bacteriologists have reported a high percentage of non-sterility. In England, Bulloch found more than 75 per cent of the sutures of eight manufacturers to be non-sterile. In Germany, Knorr found that 80 per cent of commercial catgut sutures which he examined contained pathogenic and non-pathogenic bacteria. In the United States, Meloney and Chathfield found that the products of seven suture manufacturers contained living bacteria. In a 2½ year study (2) of the possibility of sterilizing catgut by chemical treatment, I found that copperized catgut sutures of one German manufacturer and three American manufacturers were infected with aerobic and anaerobic bacteria, also that mercurialized catgut sutures of one American manufacturer were grossly contaminated. Subsequently, a 2 year investigation (3) by me of the sterility of foreign made catgut brought to light the fact that 62½ per cent of twenty-four brands were non-sterile, including the sutures of four British manufacturers, one French manufacturer, five German manufacturers, two Japanese manufacturers, and three Spanish manufacturers. In a survey (4)

of the sterility of twelve brands of American made catgut conducted during a period of 5 consecutive years (1930-1934) I found that the products of six manufacturers were non-sterile repeatedly.

The large percentage of non-sterile catgut sutures found among the brands now marketed in the United States as well as in foreign countries emphasizes the need of rigidly testing the sterility of the sutures by a reliable method which embodies adequate controls. This subject is of vital importance to the surgical and hospital professions, for it has a direct bearing upon the welfare and life of surgical patients. Since the publication of my last paper (4) on catgut sterility I have received numerous requests for a description of a reliable method for testing the sterility of catgut sutures, and it is hoped that the present paper will furnish the desired information.

## IMPORTANCE OF CHEMICAL ANALYSES

As a result of their study of the sterility of catgut sutures Meloney and Chatfield proposed a so called standard test (7) which they recommended for use by catgut firms and hospital laboratories. However, in applying this bacteriological test in connection with my study of chemically sterilized catgut sutures, I found (2) that the neutralizing solution was inadequate for removing large amounts of copper salts and mercury compounds with which some commercial sutures were found to be impregnated. During that research study I showed the fallacy of depending upon any method for testing the sterility of catgut sutures unless the details of the chemical treatment to which they may have been subjected is known.

Therefore, before applying bacteriological tests to catgut sutures, I pointed out (2) that *'careful qualitative and quantitative chemical analyses of some of the sutures must first be made to ascertain the nature and amount of the chemical compound used to impregnate the*

**Sutures.** Four sutures of any one lot are required for the purpose of making a complete chemical analysis. Then a suitable neutralizing fluid must be devised and used to dissolve and remove the particular chemical substance found in the catgut sutures and which, if not removed, might inhibit bacterial growth. When applying bacteriological tests, it has been my custom to test not less than four sutures for the presence of aerobic bacteria and four other sutures of the same lot for the presence of anaerobic bacteria, thus using not less than eight sutures for the bacteriological tests. These eight sutures, together with the four required for chemical analyses, make a minimum of one dozen required for obtaining accurate information concerning the sterility of any one lot of sutures.

A complete set of controls is essential if the bacteriological test is to prove efficient and reliable. In addition to the controls which have been used and recommended by other bacteriologists when testing sutures for sterility I have demonstrated (3) that three other controls are required if the test is to be adequately safeguarded. These will be included in the description of my technique.

#### A RELIABLE TEST

The bacteriological test outlined below is based primarily on the technique devised in 1936 by Dr. Benjamin White, and successfully used by him for several years for testing the sterility of catgut sutures. It also embodies the essentials of the method proposed by Meleney and Chatfield and that specified in the Therapeutic Substances Regulations of 1930 adopted by Great Britain.

The efficiency and the reliability of my test have been demonstrated over a period of 3 consecutive years (1930-1934) during which time it has been applied in testing the sterility of 13,522 surgical sutures comprising twenty four foreign brands, twelve American brands, as well as several thousand experimental sutures. During this time, the use of this test has successfully detected non-sterility of 63.5 per cent of twenty four foreign brands and 50 per cent of twelve American brands and it has made it possible for me to demonstrate the fallacy of chemical sterilization of catgut

sutures by revealing non-sterility of the 334 experimental lots which were subjected to the action of twenty-seven different chemical compounds under a wide variety of conditions.

**Culture medium.** The culture medium devised by Novy in 1893 and so successfully used by him since that time for anaerobic work is used. This consists of bacteriological nutrient broth prepared by infusing one half kilogram of beef for each liter of culture medium. To the broth are added 1 per cent peptone (Bacto Difco), 1 per cent sodium chloride, and 1 per cent glucose. To one-half of the medium (to be used for anaerobic tests) are added 3 per cent gelatin (Gold Medal) and 1/10 per cent litmus. The preliminary reaction is adjusted to a hydrogen-ion concentration of pH 7.6 so that after sterilization the final reaction will be pH 7.4-7.4. The medium is filtered and distributed in 40 cubic centimeter amounts into test tubes which are plugged with gauze-wrapped non-absorbent cotton and sterilized in the autoclave at twenty pounds pressure (125° C.) for 30 minutes.

A similar number of test tubes each containing 40 cubic centimeters of distilled water and an equal number each containing 40 cubic centimeters of a neutralizing solution, are plugged and sterilized in the same manner.

**Neutralizing fluids.** These solutions are employed for dissolving and removing various chemical substances used in the treatment of the catgut itself or in the tubing fluid. Unless these chemicals are removed from the catgut so that their action is completely neutralized, they will be carried over into the culture medium where they will inhibit growth of bacteria that may be contained within the catgut. These fluids should comprise at least the following three formulas:

A. One per cent sodium thiosulphate and 1 per cent sodium carbonate in distilled water. This is the only neutralizing fluid required in testing the sterility of some brands of catgut sutures, and constitutes part of my regular technique. It will remove the usual chemical substances commonly found in tubing fluids and with which catgut may be impregnated—if not present in too great an amount.

*B* Ten per cent solution of sodium thiosulphate in distilled water. This neutralizing fluid is required as a preliminary additional step in the technique if chemical analyses show that the sutures contain more than 2 per cent of a mercury compound or more than 5 per cent of iodine. In my research studies (2) on the chemical sterilization of catgut, I demonstrated that the large amount ( $3\frac{1}{2}$  per cent) of a mercury compound with which the sutures of one American manufacturer were impregnated, could not be removed with a neutralizing solution of 1 per cent sodium thiosulphate nor even with a 5 per cent solution, but that a 10 per cent solution of sodium thiosulphate would effectively remove all of the mercury compound.

*C* Five per cent ammonium chloride in distilled water with  $\frac{1}{2}$  per cent ammonium hydroxide. This neutralizing fluid is required as a preliminary additional step in the regular technique if chemical analyses show that the sutures contain copper salts even though present in very small amounts. Again, in my earlier research studies (2) I found that copper salts cannot be removed from catgut with neutralizing solutions containing either 1 per cent, 5 per cent, or 10 per cent sodium thiosulphate. After using many chemical solutions and making many tests, I found that copper salts can be entirely dissolved and removed from catgut by using the special neutralizing solution of ammonium chloride and ammonium hydroxide.

*Anaerobiosis* The anaerobic seal originally devised by Hall is used because it effectively prevents evaporation as well as the re-absorption of oxygen. This seal consists of a mixture of equal parts of vaseline and paraffin ("vaspar") having a melting point of 53 degrees C., and is sterilized in the autoclave at twenty pounds pressure ( $125^{\circ}$  C.) for a period of  $1\frac{1}{2}$  hours.

#### TECHNIQUE OF TEST

The exterior of the suture tubes is sterilized chemically by submerging the tubes for 24 hours in an active germicidal solution, such as  $\frac{1}{2}$  per cent potassium mercuric iodide. The tubes are then removed and placed between sterile towels.

The actual transfer of the sutures is made with a pair of obstetrical dressing forceps which has been boiled for one-half hour, then immersed in ethyl alcohol and thoroughly flamed. Between each transfer the forceps is immersed in alcohol and thoroughly flamed.

Two operators wearing sterile caps, face masks, gowns, and rubber gloves work together and make transfers preferably in a dustproof air conditioned chamber. After breaking the tube at the fracture mark, the strand of catgut is transferred to a test tube containing 40 cubic centimeters of sterile distilled water. As the transfer is being made, the cotton plug is removed from the test tube and the mouth of the tube is flamed. Then the tube is incubated for 24 hours. The purpose of this step is to permit the strand of catgut to absorb moisture and swell and partially untwist, thus permitting the neutralizing fluid in the next step to gain ready access to the interior of the strand.

Next, the strand of catgut is transferred to a test tube containing a sterile solution of 1 per cent sodium thiosulphate and 1 per cent sodium carbonate in distilled water, and is then incubated for 24 hours. The carbonate in this neutralizing fluid favors the continued swelling of the catgut, while the thiosulphate dissolves and removes the usual chemical substances, such as mercury, iodine, and chloramine (if not present in too great a quantity), with which the catgut may have been impregnated.

Then the catgut is transferred to a test tube of the culture medium, and those tubes which are to be incubated anaerobically are sealed with a layer 3 centimeters thick of the "vaspar" mixture. (The tubes of culture medium for the anaerobic tests are heated in the Arnold sterilizer at 100 degrees C. for at least 30 minutes to drive off oxygen, quickly cooled, promptly planted with the catgut sutures and immediately sealed to prevent return of oxygen.) All culture medium tubes are incubated for 15 days and examined daily for growth.

*Preliminary additional steps* If chemical analyses show that the sutures contain more than 2 per cent of a mercury compound or more than 5 per cent of iodine, the suture

## SURGERY GYNECOLOGY AND OBSTETRICS

strands to be tested for sterility must be transferred first to test tubes containing a sterile solution of 10 per cent sodium thiosulphate and then incubated for 24 hours. This special neutralizing fluid is used as a preliminary additional step to my regular bacteriological technique so that the sodium thiosulphate will be removed from the sutures by the distilled water which constitutes the first regular step of the technique, and thus will not be carried over into the culture medium where it might inhibit bacterial growth.

Whenever chemical analyses reveal the presence of copper salts in the sutures, a special neutralizing fluid consisting of 5 per cent ammonium chloride with  $\frac{1}{2}$  per cent ammonium hydroxide must be used as a preliminary additional step to my regular bacteriological technique. The sutures should first be transferred aseptically to tubes containing this sterile neutralizing fluid and then incubated 24 hours. Then, they must again be transferred aseptically to tubes of this special neutralizing solution and again incubated 24 hours so that the sutures will thus receive two treatments in the sterile ammonium chloride and ammonium hydroxide solution. Next, the sutures are put through the regular bacteriological technique already outlined.

**Controls:** 1 All culture medium tubes, immediately after sterilization are incubated 3 days to bring out any gross contamination before being used in the test.

2 To prove the absolute sterility of the culture medium a quantity of tubes not planted with catgut, equivalent to 3 to 5 per cent of the tubes of culture medium used is incubated for the full length of the test.

3. The growth-promoting properties of the culture medium are controlled by a series of tubes planted with decimal dilutions of an active culture of *Clostridium sporogenes*, and growth should appear in the tube containing a dilution of 1:700,000 of the original culture otherwise the culture medium is inferior for supporting bacterial growth.

4. In order to prove that chemical substances in sufficient strength to inhibit bacterial growth have not been carried over into the tubes of culture medium the test organism (*Clostridium sporogenes*) is transplanted into

tubes which have remained negative throughout the duration of the test.

In order to safeguard the test by eliminating the possibility of falsely positive results, the following additional controls are essential:

5 Two tubes of culture medium are planted with 10 cubic centimeters of each lot of distilled water and incubated for 15 days to determine the sterility of the solution.

6 Two tubes of culture medium are planted with 10 cubic centimeters of each lot of neutralizing solution used and these tubes are incubated for 15 days to determine the sterility of the solution.

7 Two tubes of culture medium not planted with catgut but sealed with a layer 3 centimeters thick from every batch made of the vapor mixture are incubated 15 days to determine the sterility of the anaerobic seal.

## SUMMARY AND CONCLUSIONS

1 Before applying bacteriological tests to catgut sutures, complete chemical analyses of at least four sutures of any lot should be made to determine the nature and amount of the chemical compound with which the sutures may be impregnated.

2 Suitable neutralizing fluids must be devised and used to dissolve and remove the particular chemical substance found in the sutures, and which otherwise might inhibit bacterial growth. Three satisfactory neutralizing solutions for various chemicals are described.

3. Not less than eight sutures of the same lot should be tested bacteriologically if accurate information is desired concerning their sterility.

4. A reliable bacteriological test is described in detail including the materials used, the actual steps of the technique, and a complete set of controls.

5 The efficiency and reliability of this test have been demonstrated over a period of 5 consecutive years (1930-1934) during which time it has been employed in testing the sterility of more than twelve thousand surgical sutures. The test has successfully detected non-sterility of 63 $\frac{1}{2}$  per cent of twenty-four foreign brands and 50 per cent of twelve American brands and it has revealed non-

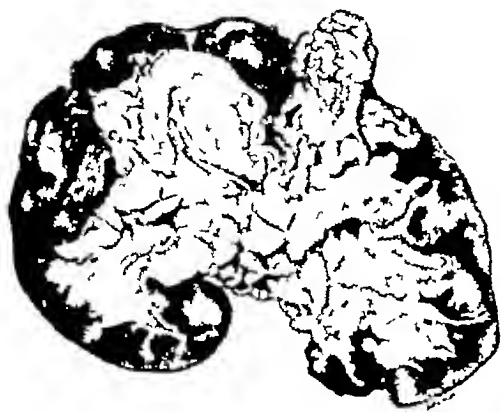


Fig. 1. Peripelvic lipomatosis—in a case of chronic glomerulonephritis with renal contracture. The peripelvic fat shows a definite proliferation and gives the impression of having crowded into the kidney substance from the hilus. Autopsy specimen.



Fig. 2. Perirenal fibrolipomatosis—in a case of multiple purulent infarcts of the kidney. The fibrosed fatty capsule and the underlying fibrous capsule are firmly adherent to the surface of the kidney. Autopsy specimen.

fat the topography of the renal substance and of the adjacent fat must be given due consideration. The kidney is covered by a paper thin transparent fibrous capsule or capsula propria, which is firmly attached to the renal tissue at the hilus. Elsewhere it may very easily be stripped from the kidney under normal conditions leaving a smooth glistening surface, with small isolated bleeding points. The kidney, with its fibrous capsule is surrounded by a mass of adipose tissue or fatty capsule, which is several centimeters in thickness. This is divided into small lobules by fine friable septa of connective tissue which are loosely attached to the capsula propria. The fatty capsule is also attached loosely to the peritoneum on the one hand and to the retrorenal fascia on the other. Thus the fatty capsule serves not only to envelop the kidney but also to support it. Under normal conditions the fatty capsule has a loose friable consistency so that the kidney, with its surrounding capsula propria, may very easily be shelled out of it by blunt dissection.

Surrounding the pelvis and the ureter, there is a thin layer of adipose tissue which closely resembles the fatty capsule in its gross and microscopic structure, and extends in a thin sheath about the calyces to their point of attachment to the renal papilla. The peripelvic fat also extends into the kidney as a thin

layer surrounding the renal blood vessels and their ramifications. The fatty capsule (perirenal fat) and the peripelvic fat are more or less continuous with one another. In every case the perirenal and the peripelvic fat as well as all projections of the latter are sharply demarcated and separated from the kidney tissue proper.

#### LIPOMATOUS HYPERPLASIA

Various pathological conditions (benign nephrosclerosis, chronic glomerulonephritis, chronic pyelonephritis and others) may eventually lead to a contracture of the kidney. The organ then shrinks leaving a rough granular surface to which the fibrous capsule is more or less firmly adherent. The renal tissue also retracts from the hilus leaving an appreciable space defect which is filled by a proliferation of the peripelvic fat. The latter then gives the impression of having crowded into the kidney from the hilus and of having replaced the shrunken renal tissue (Fig. 1). Careful gross and microscopic sectioning in every case, however, reveals that the hyperplastic adipose tissue is sharply demarcated from the renal tissue proper. Such a hyperplasia is a passive process rather than an active one. It is not

# SURGERY GYNECOLOGY AND OBSTETRICS

## PERIRENAL AND PERIPELVIC FIBROLIPOMATOSIS

### THEIR RELATION TO REPLACEMENT LIPOMATOSIS OF THE KIDNEY

FREDERICK LIEBERTHAL, M.D. CHICAGO, ILLINOIS

IN recent years numerous reports have appeared in the literature of cases of replacement lipomatosis of the kidney. This condition, which consists essentially of a replacement by hyperplastic adipose tissue of smaller or larger areas of the renal substance is said to be very uncommon. Some authors (Hillman Elnakky) maintain that the hyperplasia of the perirenal and peripelvic fat is the primary pathological process and leads secondarily to pressure atrophy of the renal substance while others (Young Kretschmer) believe that the proliferation of the adipose tissue is secondary to chronic inflammatory changes in the renal tissue itself. The latter theory is supported by the fact that replacement lipomatosis is frequently associated with a calculous pyonephrosis or with a chronic suppurative process in the kidney. But cases are described in which histological examination of the renal tissue showed merely an "atrophy and no sign whatever of any inflammatory changes. Such cases present a serious problem and have done much to arouse considerable speculation as to the true etiology of the process.

A study of each given case of replacement lipomatosis of the kidney reveals considerable destruction and shrinkage of the renal tissue large areas of which seem to have been replaced by adipose tissue which shows a smaller or greater degree of fibrosis. Histological study of the renal tissue frequently shows low grade chronic inflammatory changes. Such a specimen obviously represents an end stage of renal pathology which lead eventually to considerable destruction and scarring of the renal tissue. A careful study of the final lesion gives no clue as to the nature the sequence or the severity of the various pathological processes which may have preceded. For these may long before have run their course and vanished, leaving in their wake only reparative

changes in the form of a contracture and fibrosis, which represent the final lesion. An attempt to reconstruct the pathological development from a perusal of the individual specimen is therefore, apt to lead to false conclusions. In examining various forms of renal pathology on a large material, however it becomes evident that certain cases resemble one another and upon very careful scrutiny they prove to be various stages in the development of the same pathological process. If the cases prove to be sufficiently numerous and varied, it may be possible in this manner accurately to reconstruct the development of the lesion from its earliest to its latest stages.

We have followed this plan of attack in studying renal replacement lipomatosis.

#### SOURCE OF MATERIAL

In routine pathological examinations on a large surgical and postmortem material several thousand kidneys representing a great variety of renal pathology were subjected to careful histological study. From these over a hundred cases in which the perirenal and peripelvic fat showed significant changes, were selected for this study. In each case the topographical relation of the adipose tissue to the renal substance proper and the causal relation of the histological changes in the kidney to those in the adjacent fat were kept constantly in mind. Since the material examined is so large it will not be possible to give a detailed report of each individual case. It will therefore be the purpose of this paper to present the fundamental pathological changes as they occur in the various cases to show their relationship to one another and to trace their development from their onset to their end stages.

#### THE TOPOGRAPHY OF THE PERIRENAL AND PERIPELVIC FAT

In order accurately to follow the progressive changes in the perirenal and in the peripelvic



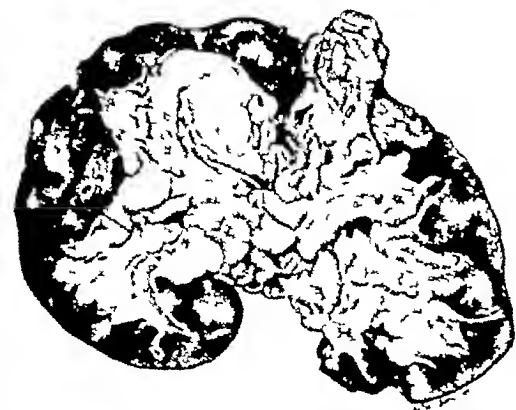


Fig. 1 Peripelvic lipomatosis—in a case of chronic glomerulo-nephritis with renal contracture. The peripelvic fat shows a definite proliferation and gives the impression of having crowded into the kidney substance from the hilus. Autopsy specimen



Fig. 2 Perirenal fibrolipomatosis—in a case of multiple purulent infarcts of the kidney. The fibrosed fatty capsule and the underlying fibrous capsule are firmly adherent to the surface of the kidney. Autopsy specimen

fat, the topography of the renal substance and of the adjacent fat must be given due consideration. The kidney is covered by a paper thin transparent fibrous capsule, or capsula propria which is firmly attached to the renal tissue at the hilus. Elsewhere it may very easily be stripped from the kidney under normal conditions, leaving a smooth, glistening surface, with small, isolated bleeding points. The kidney, with its fibrous capsule is surrounded by a mass of adipose tissue, or fatty capsule, which is several centimeters in thickness. This is divided into small lobules by fine, friable septa of connective tissue which are loosely attached to the capsula propria. The fatty capsule is also attached loosely to the peritoneum on the one hand and to the retrorenal fascia on the other. Thus the fatty capsule serves not only to envelop the kidney but also to support it. Under normal conditions the fatty capsule has a loose, friable consistency so that the kidney, with its surrounding capsula propria, may very easily be shelled out of it by blunt dissection.

Surrounding the pelvis and the ureter, there is a thin layer of adipose tissue, which closely resembles the fatty capsule in its gross and microscopic structure, and extends in a thin sheath about the calyces to their point of attachment to the renal papillae. The peripelvic fat also extends into the kidney as a thin

layer surrounding the renal blood vessels and their ramifications. The fatty capsule (perirenal fat) and the peripelvic fat are more or less continuous with one another. In every case the perirenal and the peripelvic fat as well as all projections of the latter are sharply demarcated and separated from the kidney tissue proper.

#### LIPOMATOUS HYPERPLASIA

Various pathological conditions (benign nephrosclerosis, chronic glomerulonephritis, chronic pyelonephritis and others) may eventually lead to a contracture of the kidney. The organ then shrinks leaving a rough granular surface to which the fibrous capsule is more or less firmly adherent. The renal tissue also retracts from the hilus leaving an appreciable space defect which is filled by a proliferation of the peripelvic fat. The latter then gives the impression of having crowded into the kidney from the hilus and of having replaced the shrunken renal tissue (Fig. 1). Careful gross and microscopic sectioning in every case, however reveals that the hyperplastic adipose tissue is sharply demarcated from the renal tissue proper. Such a hyperplasia is a passive process rather than an active one. It is not



Fig. 3. Mottled thickening of the capsula propria in case of calculus pyelonephritis

peculiar to the kidney and is not infrequently seen in other parts of the body, notably in the muscular tissues, when the latter undergo atrophy or shrinkage and the fat surrounding the muscle sheaths undergoes a hyperplasia to fill the ensuing space defect (hyperplasia *ex vacuo*).

But the perirenal and the peripelvic fat may undergo an active hyperplasia under the stimulus of a low grade inflammatory process secondary to a chronic inflammation in the kidney.

#### FIBROLIPOMATOSIS OR LIPOSCLEROSIS

In the presence of a low grade chronic suppurative process in the kidney (chronic pyelonephritis, infected hydronephrosis, pyonephrosis) secondary inflammatory changes may appear in the perirenal and peripelvic fat which lead eventually to a fibrosis of the adipose tissue. In the early stages (which are encountered during pyelotomy for stone or nephrectomy for a mildly infected hydronephrosis) histological examination of the fatty capsule or of the peripelvic fat reveals low grade chronic inflammatory changes in the form of a small round cell infiltration especially in the fine fibrous septa between the

fat lobules (Figs. 6 and 8). As the process advances the fibrous septa become thickened by an active proliferation of collagenic fibers and fibroblasts (Fig. 7). Gradually the connective tissue spreads into the lobules breaking them up into smaller areas (Fig. 8). Finally the entire fatty capsule becomes transformed into a firm fibrous sheath which surrounds the kidney like an armor plate (Fig. 9).

The sclerosed adipose tissue may then undergo a hyalinization which lends it a whitish glistening appearance. Occasionally calcification or a metaplasia to hyaline cartilage or even to bone is also observed.

While these changes are progressing in the perirenal and peripelvic fat a similar fibrosis is simultaneously occurring in the capsula propria. The latter which under normal conditions is as thin as tissue paper and transparent, gradually becomes more firm and opaque and may eventually reach a thickness of several millimeters (Fig. 3). At the same time the pronounced thickening of the fibrous septa of the fatty capsule which attach the latter to the capsula propria, causes the latter to become frozen into a firm fibrous mass. If it becomes necessary to extirpate such a kidney because of the underlying pathology (pyonephrosis) a plane of cleavage can be found only between the capsula propria and the surface of the kidney (intracapsular nephrectomy). The organ is then easily shelled out from the surrounding fibrous mantle until the hilus is reached. Since the capsula propria is firmly adherent to the renal tissue at this point the capsule must be incised to expose the peripelvic fat which surrounds the renal vessels and the pelvis. After the peripelvic fat is pushed back the clamps may usually be applied with ease and the kidney may be removed.

The sclerotic changes are usually more pronounced in the perirenal than in the peripelvic fat and it is this fact which renders intracapsular nephrectomy a comparatively easy procedure in skilled hands in most cases. Occasionally however the sclerosis of the peripelvic fat is so marked that exposure of the pedicle can be accomplished only by sharp dissection. But fortunately this procedure is

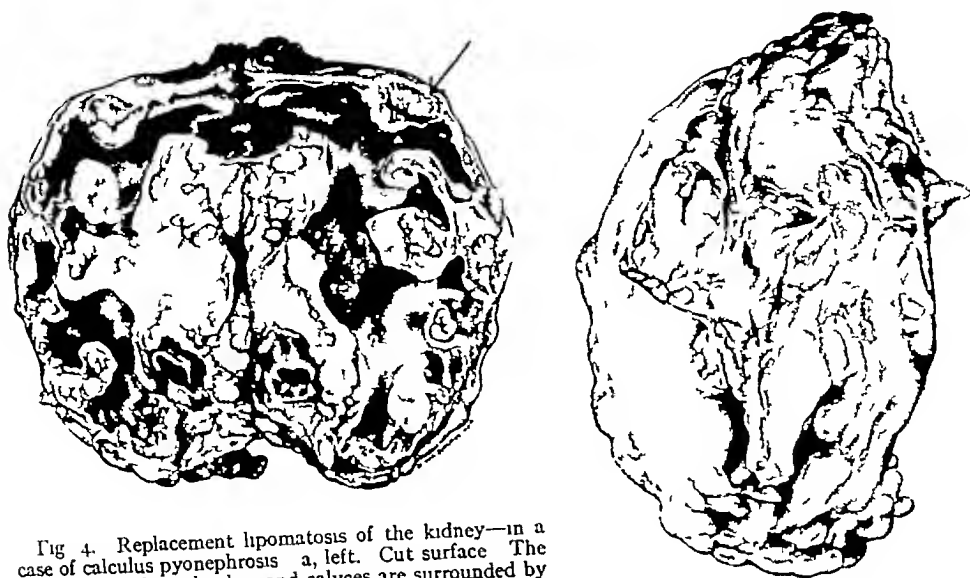


Fig. 4. Replacement lipomatosis of the kidney—in a case of calculus pyonephrosis a, left. Cut surface. The greatly dilated renal pelvis and calyces are surrounded by a tremendous proliferation of peripelvic fat which has undergone considerable fibrosis and hyalinization. The contracted renal substance has been reduced to a mere shell (indicated by arrow) which covers the pathological adipose tissue like a capsule b, Outer surface. The fibrosed fatty capsule and the thickened fibrous capsule are frozen into a solid fibrous sheath which is firmly adherent to the contracted shell of renal tissue. Removal of the kidney was accomplished only by extracapsular sharp dissection during which the vena cava was torn. Suture Recovery

not infrequently rendered less hazardous due to the fact that the pathological changes in the kidney have led to a severe renal contracture with a secondary shrinkage and obliteration of the renal blood vessels

#### CHRONIC PYELONEPHRITIS WITH RENAL CONTRACTURE AND ITS RELATION TO FIBROLIPOMATOSIS AND REPLACEMENT LIPOMATOSIS IN VARIOUS SURGICAL CONDITIONS OF THE KIDNEY

*Simple pyelonephritic contracture of the kidney*—An acute pyelonephritis tends to heal because the copious secretions of the kidney continue to wash the infected material out of the renal tubules. But if the suppuration is maintained over longer periods of time by a constant reinfection from distant foci (prostate and seminal vesicles, intestinal tract sinuses, etc.) or by a faulty drainage of the infected urine from the renal pelvis a contracture of the kidney may eventually occur. The tubuli are first destroyed and disappear, and this is followed by an atrophy and hyalinization of the corresponding glomeruli (inac-

tivity atrophy). Since a large part of the renal tissue is supplied with blood by the vasa efferentia of the glomeruli, a destruction of the latter produces a severe ischemia, which together with the secondary inflammatory changes in the interstitial tissue leads to a contracture and fibrosis of the kidney. The organ then shrinks, leaving a rough granular surface, and the renal tissue retracts markedly from the hilus. On cut section the renal substance manifests a definite narrowing, especially in the cortex. The cortical and medullary markings are usually indistinct. The peripelvic fat shows a definite proliferation and gives the impression of having crowded into the kidney from the hilus. A definite fibrosis is usually present in the fatty capsule and to a lesser degree in the peripelvic fat. Histological examination of such a kidney usually reveals definite traces of the preceding suppurative process but if the latter has run its course many months or years previously, one may find only numerous hyalinized glomeruli and a fibrosed interstitial tissue containing a few dilated tubules with a flattened epithelium

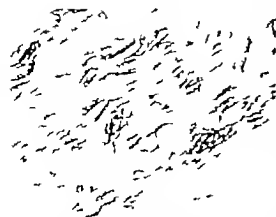


Fig. 9. Peripelvic fibrolipomatosis. High power photomicrograph shows an almost complete fibrosis of the peripelvic fat. Only a few scattered fat cells are still visible.



Fig. 10. Old pyelonephritic contracture of the kidney. Most of the glomeruli are completely hyalinized. The few remaining renal tubules are dilated and filled with caseated colloid. The blood vessels are thickened and show degenerative changes. Little inflammatory changes are no longer demonstrable. Low power photomicrograph.

fused with various neoplasms of the perirenal and peripelvic fat, of the fibrous capsule and of the renal substance proper. It is significant that such tumors may reach enormous proportions without producing any appreciable pressure atrophy of the renal tissue. Histological examination therefore reveals a perfectly normal kidney substance. In perirenal fibrolipomatosis and in renal replacement lipomatosis, on the other hand, a pyelonephritic contracture is always demonstrable and one usually also finds traces of the preceding suppurative process in the kidney.

Simple lipomata of the kidney are usually small and situated in the cortex. They are well encapsulated and separated from the peripelvic fat by a heavy wall of normal renal tissue. Occasionally however such a growth may reach such a size that it occupies an entire pole of the kidney. The calyces of the involved portion then seem to end blindly in the tumor tissue. But in such a case careful gross and microscopic sectioning will reveal that the neoplasm is well encapsulated and sharply demarcated from the peripelvic fat.

If the growth of the above mentioned tumors is infiltrative some confusion may arise on gross examination. But histological study will immediately reveal the blastomatous nature of the process.

In various forms of nephrosis the existing lipemia produces an infiltration of the renal

tissue (mainly of the proximal convoluted tubules) with chemical fat. This lends the organ a yellow color. This condition, which is sometimes spoken of as a liposis, should never be confused with lipomatosis which represents an extrarenal proliferation of actual adipose tissue.

#### SUMMARY AND CONCLUSIONS

It is generally assumed that replacement lipomatosis of the kidney is a rare condition. But comparative pathological studies show that it is merely an advanced form of peripelvic fibrolipomatosis, which accompanies every chronic suppurative process in the kidney to a lesser or greater degree. This latter condition represents a combination of a hyperplasia and a fibrosis of the peripelvic fat, occurring in response to a chronic suppuration and contracture of the kidney. In its advanced form the peripelvic fat gives the erroneous impression of having undergone a tremendous active proliferation and of having crowded into the renal substance producing a pressure atrophy and destruction of the latter. Actually the changes in the peripelvic fat are secondary to those in the renal substance proper. Careful histological examination of the renal tissue in such cases will usually reveal a pyelonephritic contracture and traces of the preceding sup-

purative process (pyelonephritis). Occasionally, however, if the latter has run its course many months or years previously, no signs of any previous inflammatory change may be demonstrable and it may then be very difficult to recognize the changes in the renal tissue as being definitely due to a previous suppurative process. Such conditions are especially apt to be encountered in the most advanced cases of replacement lipomatosis, and it is this fact which has led to the erroneous assumption by some authors that the changes in the kidney are those of a pressure atrophy due to an active overgrowth of the peripelvic fat.

All portions of the pathological adipose tissue in renal replacement lipomatosis are directly continuous with the rest of the peripelvic fat, and they are sharply demarcated from the renal tissue proper.

The development of a renal replacement lipomatosis depends upon the presence in the kidney of a low grade, chronic, suppurative process over a period of years. The circumstances which tend to maintain such a process are best encountered in cases of long continued incomplete obstruction to the outflow of the urine from the renal pelvis. This explains why renal replacement lipomatosis is so frequently seen in cases of renal stone.

Renal replacement lipomatosis must be sharply differentiated from neoplasms of the perirenal and peripelvic fat of the fibrous capsule of the kidney and of the renal substance. It should not be confused with liposis which is an entirely different pathologic entity.

Perirenal fibrolipomatosis and renal replacement lipomatosis (advanced form of peripelvic fibrolipomatosis) assume clinical importance only from the fact that they produce very extensive alterations in the topography of the tissues surrounding the kidney. A detailed knowledge of these changes is essential to the proper performance of operations on the kidney.

#### REFERENCES

1. BACON, L. H., and LE CORNET, E. R. Fat replacement of the kidney in chronic suppurative pyelitis. *Tr Chicago Path. Soc.*, 1928, 13: 25.
2. BORST, M. *Die Lehre von den Geschwulsten*. Wiesbaden, 1902.
3. ELANSEY. Lipomatosis peri-renal, cum atrophie et substitutione adiposa renis. *Ztschr f urol. Chir.*, 1929, 26: 351.
4. FURNISS, H. D. Fatty degeneration of the kidney due to calculus. *Med Rec.* 1915 37: 77.
5. GIMPELSON, E. Zur Frage der Fett Substitution der Nieren. *Ztschr f urol. Chir.* 1929, 26: 651.
6. GRIFFON, V. Atrophie et Adipose de Reins Calculeux. *Bull. Soc. Anat. de Par.* 1885 10: 360.
7. HUNT, V. C., and SMITH, H. E. Peri renal and intra renal lipoma. *Am. J. Surg.* 1928 4: 360.
8. ISRAEL, J., and ISRAEL, W. *Chirurgie der Niere und des Harnleiters*. Leipzig 1925.
9. KRETSCHMER, H., and PIERSON, L. Fibrolipomatosis of the kidney. *Illinois M. J.*, 1932 61: 356.
10. KUTZMAN, A. Replacement lipomatosis. *Surg., Gynec. & Obst.* 1931 52: 690.
11. LOWER, W. E., and BELCHER, G. W. Massive lipoma of the kidney. *Surg. Gynec. & Obst.* 1927 45: 1.
12. MATSUKAWA. Contributions to the pathology of lipomatosis. *J. Path. & Bacteriol.* 1915 20: 100.
13. RICKARDS, E. Remarks on fatty transformation of the kidney. *Brit. M. J.* 33, 2: 2.
14. WHITE, E. W., and CAMBRIDGE, H. S. Lipomatosis of the kidney with report of a case. *J. Urol.* 1934 31: 699.
15. YOUNG, HUGH H. Lipomatosis or destructive fat replacement of the renal cortex. *J. Urol.* 1935 29: 631.



Fig. 5. Replacement lipomatosis of the kidney—a case of calculus pyonephrosis. The greatly dilated pelvis and calyces are filled with pus and surrounded by tremendous proliferation of peripelvic fat. The contracted renal tissue has been reduced to paper thin shell which surrounds the entire mass like capsule. The specimen weighed 9 pounds. Intracapsular nephrectomy.

and filled with coagulated colloid. It may then be very difficult indeed to identify such a contracture as having been caused by a previous chronic pyelonephritis (Fig. 10).

**Primary pyonephrosis (small pyonephrosis)**  
In the course of a chronic pyelonephritis, an obstruction to the outflow of the infected urine from the renal pelvis may develop. The stagnant urine then gradually becomes transformed into pus, leading to the formation of an empyema of the ureter of the pelvis, and of the calyces above the point of obstruction. But since the preceding suppurative process has produced a sclerosis of the renal substance and a cellular infiltration of the wall of the renal pelvis and of the calyces, neither the pelvis nor the kidney tissue dilate following the development of the obstruction and a small pyonephrosis is the end-result. Histologically such a kidney presents the picture of a chronic pyelonephritis with contracture.

**Secondary pyonephrosis (infected hydronephrosis or large pyonephrosis)** When an obstruction to the outflow of the urine from the renal pelvis (due to an aberrant vessel, a congenital valve, an abnormal insertion of the

ureter, a renal or ureteral stone, etc.) appears before an infection has set in, a hydronephrosis develops first. The renal pelvis and the kidney substance may then dilate to a tremendous size and, if an infection of the retained urine subsequently occurs, the latter is gradually converted into pus, and a large pyonephrosis results. Histological examination of the renal tissue in such a case reveals the changes of a chronic pyelonephritis as well as those of a hydronephrosis. Through the combined forces of hydronephrotic atrophy and pyelonephritic contracture, the renal substance is then reduced to a thin fibrotic shell which stretches over the ends of the greatly elongated calyces like a huge canopy. This sequence of events leads to the formation of a large space defect which surrounds the renal pelvis and calyces, and which is bounded peripherally by the compressed shell of renal tissue. This space defect is filled by a proliferation of the peripelvic fat. The suppuration which is going on at the same time in the renal substance and in the renal pelvis gives rise to chronic secondary inflammatory changes in the hyperplastic peripelvic adipose tissue which gradually lead to a fibrosis and frequently to a hyalinization of the latter (Fig. 4).

Such a kidney may reach an enormous size and in extreme cases it may weigh 10 pounds or more. If the organ is cut open it soon becomes evident that by far the greatest part consists of sclerotic adipose tissue which is pierced by the greatly dilated renal pelvis and calyces, and which is covered by a thin fibrotic shell of renal tissue which surrounds it like a capsule (Fig. 5).

It is mainly such advanced cases which are known as a renal replacement lipomatosis.

#### RENAL REPLACEMENT LIPOMATOSIS

This condition consists of a hyperplasia and a sclerosis of the peripelvic fat associated with an advanced pyelonephritic contracture of the kidney. The inciting cause is always a low grade chronic suppurative process in the renal substance usually of many years duration. The primary pathology is always the chronic suppuration in the renal tissue and the resulting renal contracture. The tremendous proliferation and fibrosis of the peripelvic adipose

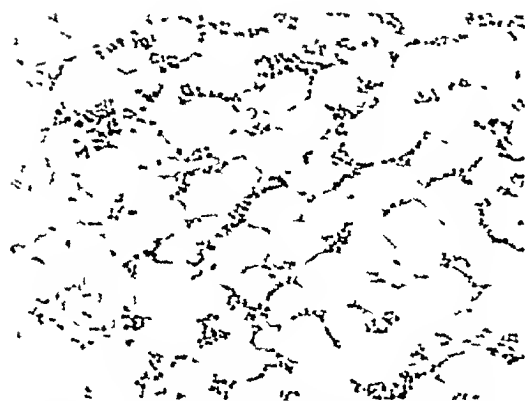


Fig. 6. Peripelvic fibrolipomatosis. High power photomicrograph showing chronic secondary inflammatory changes in the peripelvic fat

tissue is always secondary to the changes in the kidney

#### THE CLINICAL SIGNIFICANCE OF PERIRENAL FIBROLIPOMATOSIS AND OF RENAL REPLACEMENT LIPOMATOSIS

These two conditions assume clinical importance only from the fact that they produce extensive alterations in the topography of the tissues surrounding the kidney. The normal organ may very readily be shelled out by blunt dissection from its surrounding bed of adipose tissue leaving a long narrow pedicle which may be clamped and tied with ease. As the result of pathological changes in the perirenal and peripelvic fat however considerable difficulty may be encountered. In the presence of a perirenal fibrolipomatosis the fibrous capsule is firmly adherent to the sclerotic fatty capsule. A plane of cleavage may then be found only between the fibrous capsule and the surface of the kidney, and the renal pedicle may be exposed only after sharp division of the reflected fibrous capsule at the hilus (intra-capsular nephrectomy). In renal replacement lipomatosis (peripelvic fibrolipomatosis) a heavy band of fibrosed peripelvic adipose tissue surrounds the renal vessels like a mold. This produces a shortening and broadening of the pedicle. A preparation and narrowing of the latter for safe clamping and ligature can then be accomplished only by sharp dissection, which brings with it the danger of serious injury to the great vessels. It may truly be



Fig. 7. Peripelvic fibrolipomatosis. Low power photomicrograph showing a thickening of the interlobular septa of the peripelvic fat

said that if perirenal and peripelvic fibrolipomatosis did not exist operations upon the kidney would be technically far simpler than they sometimes are

Perirenal and peripelvic fibrolipomatosis are usually not recognized clinically. The diagnosis is commonly that of the underlying and causative pathological condition (pyonephrosis or pyelonephritic contracture of the kidney)

#### PATHOLOGICAL DIFFERENTIAL DIAGNOSIS

Perirenal fibrolipomatosis and renal replacement lipomatosis are not infrequently con-

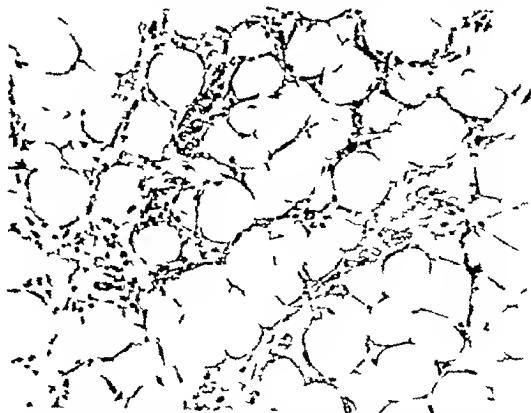


Fig. 8. Peripelvic fibrolipomatosis. High power photomicrograph showing fine strands of fibrous tissue spreading into the fat lobules and breaking them up into smaller areas

# CLINICAL SURGERY

## A SIMPLE SEVEN SUTURE METHOD OF BILATERAL URETERO-INTESTINAL IMPLANTATION

REPORT OF 12 CASES

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THE method, the surgeon, and the patient contribute in particular ways to the success of uretero-intestinal implantation. Many different methods have been used. Some of these are inherently defective and have shown a high percentage of failures no matter how skillfully performed. Others, which theoretically fulfill the requirements, frequently have failed because they were poorly executed. All methods are technical and require minute attention to every detail and some are so technical as to defeat their purpose. A perfect operation may be followed by complications arising through individual predisposition to infection, formation of stone, or other abnormality. The age and condition of the patient affect the risk and the permanence of the efficient implantation. Young people have a better expectancy and fewer diabetes than adults and the aged. The results of uretero-intestinal implantation for exstrophy and vesicovaginal fistula surpass those for vesical cancer and tuberculosis. For example. In 1924, the right and left ureters of L. P., 5 years of age, were implanted into the bowel separately (September and November) and the exstrophic bladder was removed later. The result has been perfect (Fig. 1). Two years later C. R., at the age of 6 years was treated similarly with a lasting result equally good (Fig. 2). However M. R., 33 years of age, who had lived comfortably for 4½ years after implantation, died of uremia caused by the obstruction of a stone caught in the implanted ureter of her remaining kidney—a late complication unrelated to the method of implantation.

A right tuberculous kidney was removed in 1927 followed by pyelonephritic infection. In 1928, the capacity of the bladder was only 30 cubic centimeters and the total phlebotomy per cent. The patient weighed 30 pounds and was moribund. A section removed to a peritoneal catheter but the left ureter never could be exteriorized. Left vesicopyelostomy was performed in 1929. The ureter was enlarged and dilated. No tuberculous was found at autopsy. The other result was satisfactory. The patient weighed 45 pounds within a year. She was brought to the hospital on July 1931 in a coma. At autopsy (shown) showed in the region of the left ureter. Dehydration caused by the stone. At autopsy multiple acute abscesses were found in the left kidney, but there was no evidence of tuberculous. The bladder was atrophic and almost healed. Chronic

Whereas the technique of implantation is the important part of the problem of method, the preparation and after-care of the bowel and urinary tract are equally important and special. Good abdominal relaxation is essential and an abdomen full of adhesions as the result of previous surgery presents real difficulties. The technical requirements of any method may be stated as preventive. The prevention of peritonitis, urinary leakage, ureteral obstruction, and ascending urinary infection occupies a place of artistic importance in different surgical minds, as shown by the variation in their methods of prevention. The late R. C. Coffey's efforts to avoid complications are evidenced by the idea of a functioning valve (submucosal implantation) at the point of implant to prevent ascending infection. Initial catheter drainage of the ureter to prevent obstruction from edema, abdominal packs to prevent peritonitis and take care of possible urinary leakage, and later the buried uretero-intestinal suture (third technique) for the same purpose, obviating the need of packs but obstructing the ureter until the suture forms an orifice. Higgins, using Coffey's technique III, embedded the ureter without dividing it, in the wall of the bowel with the idea of securing free drainage of urine through the natural channel until the local edema subsided and the new orifice became established by the suture cutting its way through. Both modified the Higgins technique by discarding the uretero-intestinal suture (lumen to lumen) which was not strictly aseptic, for a second stage operation at which an orifice is formed between the intact ureter and bowel by special cautery.

passive compression of the lumen, direct myomectomy, acute sphincterotomy and local sections of the ureter were found.

"The ureter is divided distal to the point which has been embedded in the wall of the bowel at previous operation. A special cautery was passed through the cut end, at the same number as embedded, to the point at which the orifice formed. An assistant compresses the peritoneum in the abdominal side of this point. The current is turned on and the wire runs through adjacent tissues and instead of the embedded orifice. The cautery makes its way and draws out through the peritoneum after it has been detached above by the surgeon. The same cautery and then the cautery and covered with paraffin or embedded.





Fig 1 Excretory urogram taken 15 years after uretero-intestinal implantation for exstrophy. Both kidneys and ureters appear normal.



Fig 2 Excretory urogram taken 13 years after uretero-intestinal implantation for exstrophy. Renal function is normal and there has been no evidence of infection.

It is possible that the factor most responsible for either good or bad results by any method, once peritonitis and local infection are conquered, is the manner of the actual implantation. The more recent methods, some of which are heretofore mentioned, are planned mainly to prevent local infection and peritonitis. Undoubtedly, such infections are grave risks. However, I feel that their prevention has been emphasized at the expense of other equally important requirements. In looking back, I found that my own failures and successes could not always be explained satisfactorily and this review led me to suspect not only that the actual manner of implantation is more responsible for the good results than the method used but also that a very marked simplification of method might lead to general improvement of results.

Omitting the details of an experimental study which will be reported elsewhere, it may be stated axiomatically (1) that the ureter should be led into the bowel by the most direct and natural route, without twisting, kinking, interference by bands, blood vessels or folds of peritoneum, too much tension or undue looseness, (2) that the incision in the muscular layers of the bowel should be made at the accessible point, in line with the natural course of the ureter and should be of suitable size, not too long or too short, exposing the surface of the submucosa (not the mucosa) without entering or breaking the blood vessels, (3) that all anchoring sutures should pass through the strong connective tissue fibers of the submucosal layer of the wall of the bowel and the adventitial

layer of the wall of the ureter without entering the lumen or even the mucosa of either, and (4) that, in closing the incision, the ureter must not be constricted in the slightest degree, and at the same time the closure must be secure enough to prevent leakage or herniation.

A very simple technique will fulfill these requirements. Certain details of the following method need refinement and further simplification. However, by it 12 patients have had both ureters implanted at one operation and the method which was used is reported as a step in the development of a technique which differs from others by its simplicity.

#### THE SIMPLE SEVEN SUTURE METHOD WITH PROBE AND CAUTERY

The method to be described may be designated as the simple seven suture method with probe and cautery, to distinguish it from a similar technique without the use of the probe, to be reported later. The steps of procedure are

- 1 The preparation of the patient,
- 2 The opening of the abdomen and the packing off of the intestines,
- 3 The preparation of the peritoneal flaps and isolation of the right and left ureters
- 4 The selection of suitable positions for the implantation and the placing of stay sutures to mark the lower of these positions,
- 5 The implantation of the ureter which is to be placed in the lower position, and then the implantation of the other ureter,



Fig. 1



Fig. 2

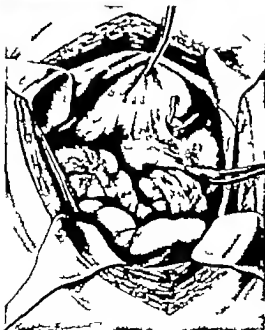


Fig. 3

Fig. 3 Drawing of the formation of the right flap of peritoneum. Each will be used to cover the site of implants.

tion of the right ureter into the pelvic cul-de-sac. The ureter is being hooked from its extraperitoneal bed by a ligature carrier.

Fig. 4 Drawing of pelvic view to illustrate the method of isolation of the ureter. Its length is made as long as desired. By traction on the rubber tape, the point of entrance into the bladder can be seen transperitoneally. Through a short incision at this point, the ureter can be exposed and pulled out.

Fig. 5 Drawing of the abdominal view of the isolation of the ureter. The dotted line on the ureter near the bladder shows the point of division. The two ends are tied, the clamps removed, and the short end in the peritoneum closed with catgut.

6 The covering of the sites of implantation with the respective flaps of peritoneum.

7 The closure of the abdomen without drainage.

The particulars of each step are important and therefore are given in detail.

*Step 1: The preparation of the patient is very important.* The following outline gives the principal points.

The patient should have a non-residue diet for at least 3 days preceding operation.

Urinary antiseptics should be given.

3 Urograms should be taken and the non-protein nitrogen of the blood should be determined.

4 Castor oil, ounce should be given day before the operation.



Fig 6 Drawing which illustrates the selection of the favorable site for implantation so that the ureter has a natural straight entrance into the bowel. The line for incision, indicated by broken line beneath the ureter is marked by stay sutures.



Fig 7 Drawing to illustrate the method of making the incision in the wall of the bowel down to the submucosa. The muscular layers can be separated from each other and stripped from the submucosa beneath by spreading open the points of a clamp in the incision.

be empty. Intestinal clamps then are unnecessary.

5 Three soap suds enemas should be given the first, early in the afternoon of the day preceding operation, the second, on the evening of the same day, the third, on the morning of operation. All of this third enema must be siphoned back.

6 No fluids should be taken after 6 a.m.

7 Breakfast should be omitted.

8 A retention catheter should be placed and left open during the operation in order that the bladder will be empty and out of the way.

Spinal anesthesia gives the best relaxation and can be reinforced with gas and oxygen or ether if necessary. Ether is better for children.

**Step 2 Abdominal exposure.** A mid-abdominal incision is made from the symphysis to alongside the umbilicus. The intestines are packed off with a rubber sheet reinforced with gauze packs. The abdomen should be relaxed and the bowel must

**Step 3 Formation of peritoneal flaps and isolation of the ureters.** The peritoneum is slit as near the pelvic colon as possible, alongside that portion into which the ureter is to be implanted, and not over the ureter. This incision is extended with scissors in both directions parallel to the gut. The outer layer then is stripped up, carefully so as not to tear it, beyond the position of the ureter both below and above the brim of the pelvis, and this flap of peritoneum is made of a sufficient size so that its edge can be drawn well out to the middle of the pelvic colon. The ureter strips up with this peritoneal flap as a rule (except in old people) and can be drawn out of its extraperitoneal bed by hooking it with a ligature carrier thrust beneath the peritoneal flap (Fig 3). A tape of soft rubber is looped over the ureter which is dissected free of the peritoneum forming the flap, care being taken to interfere as little as possible with the peri-ureteral fascia and blood vessels and not to pinch, twist, or traumatize the ureter. By gentle traction on the tape, after the bladder has been lifted up into the suprapubic wound, the juxta-



Fig. 8 Drawing illustrates the manner in which the three anchoring sutures are placed. *a*, Suture, No. 1, passed from left to right through the subcutaneous, right to left through the adventitia, care being used not to enter the lumen of the bowel or ureter. *b*, Suture, No. 2, is passed opposite No. 1, keeping in mind the principles illustrated in Figure 3. *c*, *d*, Show how each suture is placed in the subcutaneous. *d*, Shows the triangle of subcutaneous marked off by the three sutures.

vertical portion of the ureter can be seen transperitoneally. A short incision is made in the peritoneum at this point, and through this a small loop of the ureter is pulled out (Fig. 4). Then the ureter is doubly clamped, divided between the clamps, and each end is ligated (Fig. 5). The short slit in the peritoneum next to the bladder through which the ureter has been divided, is closed with catgut. By careful manipulation so as neither to traumatize nor to interfere with its blood supply

the freed and ligated end is pulled back and out from under the peritoneum. This leaves the ureter sufficiently long to enable transplantation at that point which later seems the most favorable.

A peritoneal flap is prepared and the ureter on the opposite side is isolated in a similar manner.

*Step 3. Selection of site for implantation.* After both ureters have been isolated the anatomical relationships which have been created should be

studied. The most natural course of each ureter into the bowel must be determined in relation to the flaps of peritoneum on each side which have been prepared purposely to cover the sites of implantation and, if this relationship is wrong, the flaps should be modified to correct it by extending the incision in the peritoneum either up or down. It is preferable that the ureters should not enter the bowel at the same level and usually it is easier to place the left ureter higher than the right. This point can be settled by laying the ureters over the bowel and then manipulating ureters, bowel, and flaps into various positions until that which seems to be the most favorable is found.

*Step 5. Implantation of the ureters with seven sutures.* The position for implantation is marked by two stay sutures, one at each end of the imaginary line of incision (Fig. 6). The main purpose of these sutures is to mark the line for incision. They are used very little for traction. The part of the bowel marked by the sutures is held up and smoothed flat on the fingers of the left hand with the thumb. The sense of touch helps greatly in cutting to the depth desired and straight through the layers instead of on a slant or dissecting off between layers. A clean cut from 2.5 to 3 centimeters long (4 centimeters for hydro-ureter) is made in line with the two stay sutures through the muscular coats which are teased back by blunt dissection, thus exposing the surface of the submucosa with its blood vessels in the lower two-thirds of the incision for an area from 6 millimeters wide and 2 centimeters long (Fig. 7).

The ureter now is laid over this incision and sutured (Fig. 8). It has become distended with urine in the few minutes since ligation. Attention aids in making a neat implantation: proper length, moistening, suturing through the adventitia, approximation of the lumen, and more accurate size of the triangle which will be formed by the submucosa by the three anchoring sutures. A suture of 20 day four o chromic gut is passed through the submucosa (care being taken that it does not enter the mucosa or the lumen of the bowel, Fig. 8, c) at the outer border of the area exposed, about 4 or 5 millimeters from its lower end, and then through the adventitia of the outer side of the ureter (care being taken that it does not enter the lumen or the mucosa even, flattening the ureter with the thumb on the index finger of the left hand aids in properly placing these sutures) at the proper point and side (Fig. 8, a) so that, when tied, a good fit will be secured. It is not tied at the time. The ends are left long

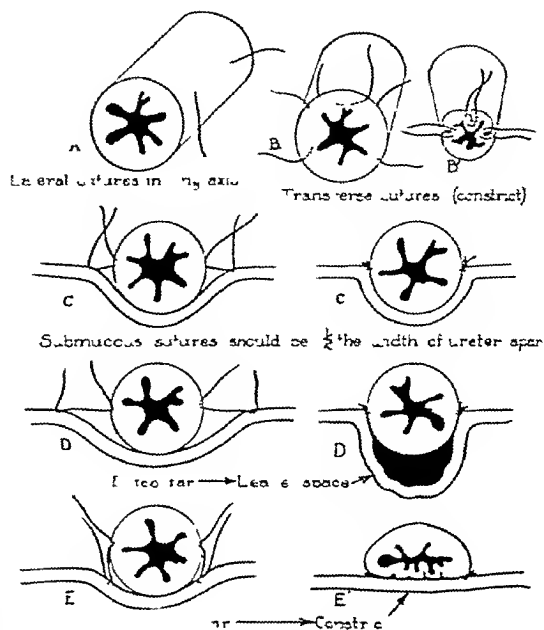


Fig. 8  
care a

presentation of the reasons for sutures. A. The right method of suturing method a transverse suture might constrict sutures should be of 1 1/2 times the diameter of the ureter thus the sutures are tight.

the place border of the triangle of which is the ureter. This thus the adventitia of the submucosa the proper relation to the



Fig. a



Fig. b

Fig. b. Drawing from another viewpoint to illustrate the method of inserting the ureter. With the probe through the opening into the bowl made by the catheter. After the ureter is inserted, the mosquito clamps with rubber guards.

Each are not shown in the illustrations, on the loops of sutures No. 1 and No. 2, are withdrawn and these sutures are drawn tight and tied, thus anchoring the ureter in position.

Fig. c. Diagrammatic representation of the manner in which the ureter is anchored in the wall of the intestine by the 4th suture. a, Shows how the suture, No. 4, and 5, anchor the ureter tightly in the small opening through the subcutaneous and mucosa made by the catheter and illustrates the reason this slit should not be too large but of size, as indicated by the dotted circle, equal to the diameter of the ureter. b, represents the uncontracted anastomosis. Ureter is secured, and c, shows how the fourth and fifth suture anchor the ureter in the trough of the anastomosis.

forms the third anchoring suture of the anastomosis to the subcutaneous. The two parts of the loop of each of the three anchoring sutures which penetrate the subcutaneous are brought together and held in mosquito clamps fitted with rubber guards. Traction on these three clamps will lift the triangular area in the subcutaneous which is to be perforated. In this way the point for perforation and insertion of the ureter can be steadied when the time comes to implant the ureter and the lifting of the wall of the bowel prevents contami-

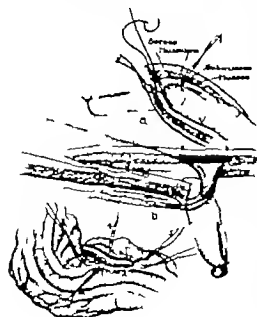


Fig. c

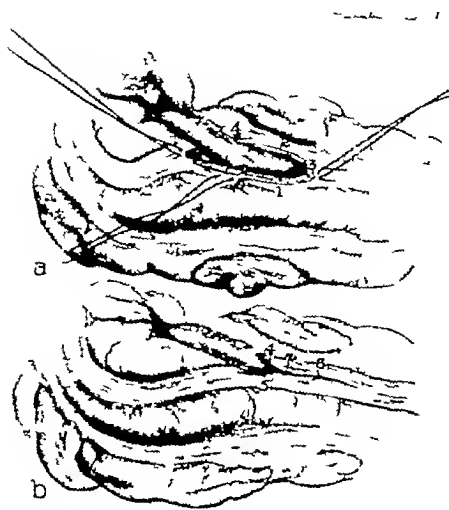


Fig 13 Drawing to show how the sixth and seventh sutures are placed. Sutures 4 and 5 do not catch the submucosa since their purpose is to hold the ureter in the muscular trough. Suture 6 should catch a small strand of submucosa on each side, since otherwise it might tear out. Suture 7 closes the serous and muscular layers only. Catching the submucous layer in this suture might cause when tied, constriction of the ureter and, since this suture is relieved of strain by suture 6, a submucous hold is unnecessary.

nation of the field by the regurgitation of any of its contents after it has been perforated. This will not occur if the bowel has been prepared properly and is empty. The distance between the three anchoring sutures in the submucosa is of some importance. The base of the isosceles triangle formed by them should approximate one and one-half times the diameter of the ureter so that when they are tied the ureter will fit the triangle. The sutures should pass lengthwise through the adventitia of the ureter, and not crosswise, in order that a good hold can be had without constricting the ureter when tied (Fig 9).

An abdominal pad now is placed over the bowel and the ureter laid on it so that when the ureter is opened no urine can soil the wound. The tied end of the ureter should reach at least 3 centimeters beyond the level of the three anchoring sutures and it may be longer. This excess length will hang free in the bowel after implantation but will slough off after several days, either flush with the anastomosis or enough so that only a small papilla remains with the permanent orifice at its base. A temporary orifice beyond the wound and the point at which the new and permanent orifice will be, prevents urinary extravasation into the



Fig 14. The method of extraperitonealization of the sites of implantation.

wound and makes the implantation easier from the technical standpoint. Ureteral obstruction from surgical edema during the first few days after operation also is less likely. About 1 centimeter from its ligated end, the ureter is slit so as to give a good, full temporary opening (0.5 to 1 centimeter in size). A probe is passed through this slit into the blind end and given to an assistant who holds the ureter on the probe by pulling up the slack with a ligature carrier (Fig 10). The gauze pad over the bowel is removed. The triangular area of submucosa is lifted taut with the three mosquito clamps, and a small opening is made with a fine cautery through it and the mucosa between the two lateral sutures. Care must be used to make this slit the size of the diameter of the ureter and not too long, as happened on one side in my last case when I used an electric knife. An incision which is too large gives a greater risk of leakage at the site of implantation.

## SURGERY GYNECOLOGY AND OBSTETRICS



Fig 5

this method (Case 5). The left renal pelvis and the right ureter appear dilated. The general condition of patient for 35 months since operation has been good (see Fig 18).



Fig 6

Fig 5 Extra-uterine pregnancy, taken at the time of discharge from the hospital, of the first patient operated on by this method (Case 5).

Fig 7 Extra-uterine pregnancy, taken at the time of discharge from the hospital, of the first patient operated on by this method (Case 5).



Fig 7

Fig 8 Extra-uterine pregnancy, taken at the time of discharge from the hospital, of the first patient operated on by this method (Case 5).



Fig 8

Fig 8 Patient with an extensive epidermoid cyst of the neck of the bladder and urethra (Case 5) 35 months after Agassiz cysto-urethrectomy (see Fig 1).



Fig 9

Fig 9 Photograph of the patient with the cysto-urethrectomy shown in Figure 6 35 months after bilateral uretero-an-



Fig 10

Fig 10 Patient with incurable congenital bacula (Case 15) 35 months after ortho-uterine implantation (see Fig 24).



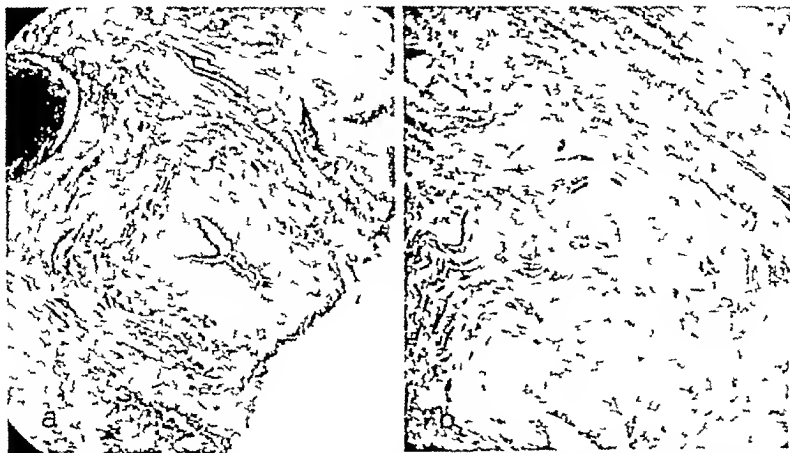


Fig 21 Photomicrograph of a section of the ureter, of the 74 year old patient (Case 3) subjected to too much surgery, where it entered the lumen of the bowel showing perireteral inflammation and constriction a, left Low power b, high power The ureter and kidney above were normal

The end of the ureter on the probe is guided into this opening by the assistant and pushed into the lumen of the bowel (Fig 11). The three mosquito clamps are removed in succession and each time the corresponding anchoring suture is drawn tight. The withdrawal of the probe is the step in technique which involves the only real risk of sepsis and a modification of technique to avoid this is being tried out experimentally. After the probe has been withdrawn carefully onto a strip of

gauze to avoid contamination of the area, these three sutures are tied.

Sutures No 4 and No 5 are used to anchor the ureter in the upper part of the muscular channel (1 to 1.5 centimeters in length) still left of the original incision. One of the cut edges of the incision is lifted in tissue forceps and a suture (suture No 4) of the same material as that used for Nos 1, 2, and 3 is passed through the serosa and muscularis of this lip without catching the



Fig 22



Fig 23



Fig 24

Fig 22 Excretory urogram of the same patient as Figure 17, taken 1 month previously

Fig 23 Excretory urogram of Case 3, 12 months after hydro-uretero-intestinal implantation. The ureteral dilata-

tion and the hydronephrosis are gradually disappearing

Fig 24 Excretory urograms taken 4 months after bilateral implantation of the ureters into the pelvic colon (Case 9). The kidneys and ureters appear normal



TABULATION OF CASES\*—Continued

Case Sex Age	Diagnosis and pathologic report	Operations	Course	Autopsy	Remarks
7 M 63	Squamous cell carcinoma of the bladder (extensive) Total phthalein 55 per cent Excretory urograms showed no dye on the left and a normal right ureter and renal pelvis	1 The left hydro-ureter was tied off but not transplanted Right uretero-intestinal anastomosis. (The opening into the bowel was made with scissors and not with cautery) Convalescence was fair with periodic deviations of temperature 2 Total prostatic cystectomy (7 weeks after transplant) Pathological examination showed extension into the prostate and left ureter A small abscess was opened into extraperitoneally in the region of the ligation of the left ureter	Sudden exitus on the fifteenth day after cystectomy 9 weeks after the transplantation	No autopsy Impression Suppurative left nephritis with perirenal and peri ureteral abscesses. Apparently the transplant on the right was working satisfactorily	The patient died of sepsis secondary to the complete obstruction of the left ureter (see Case 5)
8 M 64	Carcinoma of the prostate with extensive invasion of the bladder	Bilateral uretero-intestinal implantation The opening in the bowel was made with Skene's cautery	The patient developed bronchopneumonia on both sides and died in 5 days	No autopsy	The operation technically was good
9 F 42	Vesicovaginal fistula. Hysterectomy 4 years ago An attempt to repair the fistula has been made each year since. Excretory urogram showed normal kidneys and ureters	Bilateral uretero-intestinal implantation using Skene's cautery to open the bowel There were very extensive intestinal adhesions which had to be freed before the field could be packed off and the pelvic colon exposed	There was considerable abdominal distention on the second day urine was draining by rectal tube The temperature rose to 104 degrees on the third day and was normal by the fifth day The patient was passing gas and fecal material by the fifth day Convalescence was uneventful from then on		The patient left the hospital in good condition and much pleased to be continent again Figure 24 shows the excretory urograms and Figure 25 is a photograph of the patient
10 M 63	Carcinoma of the bladder (biopsy) fulgurated four separate times without benefit. Blood pressure 180/75	1 Bilateral uretero-intestinal implantation using Skene's cautery to open the bowel Duration 1 hour and 30 minutes 2 Retroprostate- seminal vesiculocystectomy October 27 1934	Convalescence after uretero-intestinal transplantation was uneventful Recovery after cystectomy was good The patient was up on the eighth day but developed septicemia from a pelvic abscess and died on the fifteenth day after cystectomy	Death from septicemia Cortical abscess in left kidney without pyelitis or obstruction of ureters	Excellent result of transplants (Fig 25)
11 M 72	Carcinoma of the prostate vesicles and bladder	1 Bilateral uretero-intestinal implantation using Skene's cautery to open the bowel 2 Cystectomy attempted The pelvis was frozen and it was impossible to remove all of the cancer	Convalescence good after implantation Suprapubic fecal fistula from injury of rectum when cystectomy was attempted Patient died on the fifth day after cystectomy	The ureteral ends have not sloughed off (Fig 26) There was no peritonitis or local infection	
12 F 9	Complete incontinence following an automobile accident at the age of 3 years Attempts to repair the incontinence were made at the age of 3 and again at the age of 6 without benefit When the child was examined, no vagina could be found and a uterus was not palpable. Apparently the vagina had been used to make a urethra Ureteral implantation seemed the only way to secure continence X-ray films show spina bifida of the entire sacrum and abnormal separation of the pubic bones of the symphysis. Intravenous urograms show normal kidneys and ureters	Bilateral uretero-intestinal implantation by the simple seven suture probe and cautery method An electric knife was used and the opening made by it was too large on both sides but more so on the right where an opening 1 cm long occurred necessitating suturing of the submucosa to close the bowel a procedure otherwise unnecessary	This patient had nausea and some vomiting with slight abdominal distention for 48 hours after operation The highest temperature was 38.2 degrees and the temperature was normal on the fourth day The blood urea on the second day was 28 mgm per cent The urine through the bowel was blood tinged for 48 hours but has been clear since	This patient has been seen several times since leaving the hospital and has remained in excellent condition	Figure 7 shows excretory urograms before and after operation Figure 28 is a photograph of the patient

\*The analysis of other cases operated upon by the author by different methods than the one described in this paper is given in the paper entitled Uretero-intestinal Implantation etc Surg Gynec & Obst 1915 60 1115

†At operation ovaries and an infantile uterus were found but their relation to the bladder or vagina was undetermined.



Fig. 5. Photograph of kidneys, ureters, and portion of pelvis in color, showing that the redundant ureteral ends have not sloughed off. The ureters and kidney pelvis were dilated before operation because of obstruction from cancerous invasion of the bladder (Case 4).

submucosa and then is passed longitudinally through the adventitia of the ureter at the proper lateral margin as it lies in the channel and back through muscularis and serosa, in the form of a mattress suture. Suture No. 5 is passed on the opposite side similarly through the other lip of the incision and through the adventitia of the adjacent side of the ureter. The surgeon must be absolutely certain that neither of these sutures perforates the ureter. When sutures Nos. 4 and 5 are tied, the ureter lies free and unobstructed but firmly imbedded in the muscular channel (Fig. 12).

Sutures No. 6 and No. 7 are of intestinal linen or silk (Pagenstecher). They close the lower portion of the incision (about 1 to 1.5 centimeters in length) by bringing together the cut edges of the serosa and muscular layers of the bowel over the point at which the ureter perforates the submucosal and mucosal layers. The sixth suture is placed at the level of the third anchoring suture and should catch a small strand of submucosa on each side. The seventh suture closes the muscular layers of the bowel without submucosa just above the level of the first and second anchoring sutures (Fig. 13). If properly placed, they will prevent herniation of the bowel and will not cause obstruction of the ureter. Of course, more than two sutures may be used for this purpose if necessary, as is the case if too long an incision in the bowel has been made.



Fig. 10. The pelvis and ureters are not dilated. The ureteral ends have sloughed off; the orifices into the bowel are well patent. Cortical abscess of the kidney undoubtedly hematogenous in origin, a part of the picture of general septicemia (blood culture positive) resulting from abscess in the pelvis following cystectomy.

The other ureter is implanted by the same technique as that given above.

**Step 6. Extraperitonealization.** The flap of peritoneum on the right is adjusted to cover the area where the right ureter enters the bowel and is sown in place with interrupted catgut sutures. The left side receives the same treatment. Care is taken that neither bowel nor ureter is pulled out of line by these flaps and that the direct and natural extraperitoneal course of each ureter is preserved (Fig. 14).

**Step 7. Closure.** The abdomen is closed in layers (peritoneum, fascia, connective tissue, skin) without drainage. It should be remembered that the bowel has been opened and there may have been some contamination of gloves and instruments. A complete change to a sterile set is necessary to insure against infection of the wound during closure.

#### REPORT OF CASES

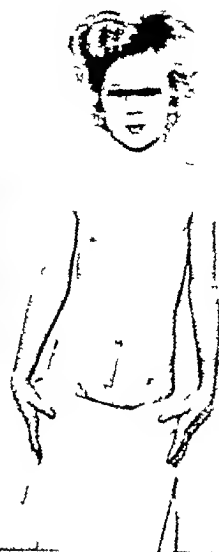
Twelve patients have had simultaneous bilateral uretero-intestinal implantation by the simple seven suture method described above. (One had eutrophy, had vesicovaginal fistula, had tuberculous cystitis; 3 had cancer of the urethra and vesical neck, and 5 had cancer of the bladder.) Five patients have died. Only one of



Fig 27, left. Excretory urograms before and after bilateral uretero intestinal implantation (Case 12) a, November 18, 1934, 11 days before operation b, December 14, 1934, 15 days after operation This roentgenogram is

of higher magnification than a, however, there is slight pelvic dilatation, particularly on the right

Fig 28 Photograph taken 2 weeks after a one stage bilateral uretero-intestinal anastomosis (Case 12)



the four deaths, however, occurred directly after the ureteral implantation (Case 8 in the table) This patient developed bilateral bronchopneumonia Unfortunately an autopsy was not obtained The ureters drained well from the beginning and the bowels were well open There was no distention and no abdominal or renal tenderness—no indication clinically of any complication which might have arisen from a fault in surgical technique

Three of the deaths (Cases 7, 10, and 11) followed an attempt to remove radically at a later time the bladder, prostate, and vesicles one of these deaths, however, apparently can be attributed to renal sepsis arising from the ligation of a large hydro-ureter It was thought safer at the time to tie it off than to implant it Had nephrectomy been performed shortly after the cystectomy, this patient might have lived There was no ascending infection on the implanted side The other death (Case 3) was the result of too much surgery at one time, bilateral transplantation and removal of the bladder and urethra Radical cystectomy for cancer carries as much risk as ureteral implantation However, a risk of less than 10 per cent for the latter will fully justify its use in order to permit an attempt to remove a cancer which is incurable otherwise All of the 5 patients who died had carcinoma which became operable only after deviation of the urine Of

the 7 patients living, 2 had cancer which was inoperable until after ureteral implantation The time is too short to know whether these 2 patients have been cured of their cancer At present both are well and show no evidence of recurrence after about 1 year The 5 other patients (1 had exstrophy, 2 had tuberculous cystitis, and 2 had vesicovaginal fistula) are all doing well

The main facts about the 12 patients are given in the table

#### SUMMARY

The foregoing results, so far as the cure of cancer is concerned, are far from satisfactory They are reported to illustrate a stage in the development of a technique of uretero-intestinal implantation which differs from others by its simplicity<sup>1</sup> When one checks the requirements of the problem of transplantation with these early results, they give some encouragement. It is too early to form an opinion about late results

In none of these twelve patients has there been any urinary or fecal leakage or sign of peritonitis Infection at the site of transplant has not been found in those who have come to autopsy There have been, however, surgical shock, 2 cases of bronchopneumonia, and some evidence of renal infection There is room for improvement

<sup>1</sup>The experimental work on dogs in collaboration with Drs. Murphy Wayman and McCorkle, which led to the clinical trial of the simple seven suture method, will be discussed elsewhere.

## ARTERIOVENOUS ANEURISM OF SUPERIOR THYROID ARTERY AND VEIN

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In spite of the frequency of thyroidectomy the occurrence of arteriovenous communications between the superior thyroid artery and vein is of great rarity. This is all the more remarkable, since the vessels are usually included in one ligature when the superior pole is ligated. In a similar anatomical situation, arteriovenous aneurisms are not uncommon in the stump of an extremity after amputation, when the artery and vein have been tied together. An interesting feature of these cases is the fact that the symptoms begin soon after operation and last for a great many years before the patient seeks relief. Because of the communication, these aneurisms rarely reach large sizes. Their chief symptom is an annoying bruit synchronous with the heart beat. This bruit is disturbing and frequently causes irritability, nervousness, and loss of sleep. They are not inherently dangerous, as they do not rupture, and they are too small to cause cardiac hypertrophy so frequent in arteriovenous communications of large vessels. After operation the relief from symptoms is immediate.

**CASE 1.** William A. Downes, 40 years of age, operated on for carcinoma, had had thyroidectomy 7 years before. She noticed throbbing in the right side of her neck 6 months after operation. The swelling was the size of goose egg. A diagnosis was made of an aneurism of the common carotid. The operation revealed large communicating sac between the superior thyroid artery and vein. The artery and vein were ligated and the sac was easily removed. The patient made satisfactory recovery.



Fig. Location of aneurism in author's case

**CASE 2.** J. M. Mera reported the case of a woman, aged 40, who had had thyroidectomy 5 years before admission. A few days after operation she noticed small swelling in the left side of the neck, which has persisted ever since. She also gave history of erysipelas. Her chief complaint was an annoying bruit, which disturbed her at night. There was a small expansile tumor 4 centimeters in diameter, 2 centimeters below the mandible. A diagnosis was made of arteriovenous aneurism of the thyroid and vein. The aneurism was removed under local anesthesia. Recovery was successful.

**CASE 3.** Selman reported the case of a white female, aged 40, who admitted with complaint of edema, shortness of breath, palpitation, cough, and nervousness. She said that she has had heart trouble for 10 years. Four years before, thyroidectomy was done. During the past year she has had very severe unproductive cough. In spite of her symptoms, cardiac examination was comparatively normal. On the left side of the neck, in the region of the upper border of the thyroid cartilage, there was a small tumor, 4th palpable thrill and loud bruit. Under local anesthesia, the sac was dissected out. It proved to be an arteriovenous communication between the superior thyroid artery and vein. The interesting feature is that, although there was single afferent artery there are numerous veins, each emptying into the jugular. Following operation, the cough and shortness of breath subsided.

**CASE 4.** Author's case. E. L., aged 44 years, was admitted to the Jewish Hospital, November 2, 1934. She was referred by the neurological clinic with complaint of nervousness and loud disturbing noise in the neck. Thirteen years before, thyroidectomy had been done. Following thyroidectomy she had aphonia for 3 months, which gradually disappeared. The best of her known knowledge appeared in the neck 1 year after operation and



Fig.

had persisted ever since. Her chief complaint was the bruit, which kept her from sleeping.

General examination revealed a comparatively normal woman. Her blood pressure was 130/80, right arm, left arm, 134/80. Laryngoscopic examination showed a flaccid left cord. Wassermann reaction was negative. On the left side of the neck, mesial to the sternocleidomastoid muscle, at the left of the superior border of the thyroid cartilage, was an expansile swelling, 2 centimeters in diameter. There was a loud bruit and a marked thrill. Pressure over the common carotid artery at Chassaignac's tubercle caused a cessation of the thrill. There was a scar, evidently of a thyroidectomy. Diagnosis of arteriovenous aneurism of the thyroid artery and vein was made.

Under local anesthesia, a longitudinal incision was made along the inner border of the sternocleidomastoid muscle. The sac was exposed, and there were found an afferent vessel leading directly from the external carotid and a single vein leading from the sac to the jugular vein. As can be seen from the drawing, the jugular vein was dilated to twice its normal size from the constant stream of arterial blood. The artery and vein were ligated with black silk and the sac easily removed. She left the hospital on the sixth day after operation.

The diagnosis in these cases is, of course, obvious. Their rarity may be estimated by the fact that in the different series of arteriovenous com-

munications collected by Braman, Callander, Makins, and Reid, no mention of this condition is found.

An exhaustive search of the literature revealed the 3 cases herein reported.

#### BIBLIOGRAPHY

1. BRAMAN, F. Das arteriell venose Aneurysma. Arch f. klin. Chir., 1886, 33: 1.
2. CALLANDER, C. L. Study of arteriovenous fistula with an analysis of 447 cases. Johns Hopkins Hosp. Rep., 1920, 19: 200-358.
3. DOWNES, WILLIAM A. Arteriovenous aneurism of the superior thyroid artery and vein. Ann. Surg., 1914, 59: 789.
4. MAKINS, G. H. On the vascular lesions produced by gunshot injuries and their results. Brit. J. Surg., 1916, 3: 353.
5. MORA, J. M. Arteriovenous aneurism of left superior thyroid vessels. Surg., Gynec. & Obst., 1929, 48: 123.
6. REID, M. R. Arteriovenous communication. Arch. Surg., 1925, 10: 601.
7. SELMAN, J. J. Arteriovenous aneurysm of thyroid vessels. Am. J. Surg., 1934, 17: 99.

A NEW METHOD OF REDUCTION OF DISLOCATIONS AT THE SHOULDER JOINT<sup>1</sup>

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On December 4, 1869, Theodore Kocher appeared before the Cantonal Medical Society at Berne and demonstrated on the cadaver his method of reduction of shoulder dislocation. Previous to this time the methods in vogue had relied chiefly upon abduction and traction in various combinations. Kocher presented his method as one employing *finesse* rather than force, making use of muscular spasm rather than combating it. It was the first thoughtful approach to the treatment of dislocation and has persisted to the present date as perhaps the one best method. Nevertheless, Kocher advised its use with certain limitations and very modestly and frankly stated that "in cases in which the head of the humerus fails to engage the glenoid fossa, other methods may be required. He believed the method contra-indicated (1) when the joint capsule was entirely torn off, especially when the upper and anterior portion of the capsule was separated, (2) when the humerus was fractured, (3) when the border of the glenoid fossa was broken. While few in number these contra-indications affect a large number of the cases of shoulder dislocation which must be treated.

In the remaining group of selected cases suitable to Kocher's maneuver it has been my experience that considerable difficulty frequently arises in obtaining reduction. Either by lack of skill or knowledge on the part of the operator or by reason of the firmness of muscular and ligamentous attachments, it is often the case that the Kocher procedure requires several trials before success is attained. Even in the instances in which reduction is obtained promptly and easily, there is considerable trauma to the joint and its surrounding soft tissues by reason of the severity of the manipulation. For this reason I have attempted, as have many others, to fashion a satisfactory substitute. By reason of its loose capsular attachment and the shallowness of the glenoid fossa, the head of the humerus rather easily slips out of its normal position. Once dislocation has become complete, it is maintained not so much by bony contours and ligamentous engagement as by muscle spasm and were the muscles removed, the head could be replaced quite as easily as it was dislocated. This can be very simply demonstrated on fresh autopsy ma-

terial. As the position of the arm in which dislocation is most frequently incurred is one of abduction, it naturally follows that this position is the one in which dislocation is most easily reduced. Others, notably Stillman, have laid emphasis upon this feature and have devised various methods with this as a basis. Employing this basic principle of abduction and traction, which is not new, I have developed the following procedure which has proved uniformly satisfactory in my hands, and which I have reason to believe can be taught easily and applied in all cases.

If there is no fracture involving the joint and if the individual is not unusually muscular, anesthesia may not be necessary. As the manipulation does not increase the trauma or the degree of pain already present, it is my practice to make one attempt without anesthesia. In cases of fracture involving the glenoid or the humerus, no attempt at reduction should be made without complete anesthesia either local or general. The patient is placed on his back upon a table, the operator standing at his affected shoulder and facing toward his feet as in Figure 1. The affected arm is then taken by the wrist and with the elbow extended is abducted to 90 degrees. The elbow of the operator is then placed against the patient's chest wall just below the axilla as in Figure 2 and the palm of his hand engages the bend of the patient's elbow (Fig. 3). Using the base of his palm as a fulcrum, the operator then further flexes the patient's arm at the elbow joint, thus making use of a powerful lever which makes controlled traction upon the dislocated humerus. The operator completes the maneuver by still further flexing the arm at the elbow and adducting the humerus to 45 degrees as in Figure 4. At times it will be found that the operator's forearm is too short to provide an adequate leverage and in this circumstance a pad of the necessary thickness is introduced between his elbow and the chest wall of the patient (Fig. 5). By this means the operator's arm can be made to fit the dimensions of any patient.

The mechanical principles involved in this maneuver are extremely simple as may be seen from the accompanying line drawing (Fig. 6). The line *DF* represents the operator's forearm which rests against the patient's chest wall at *F* and supports the hand which acts as the fulcrum





Fig 1



Fig 2



Fig 3



Fig 4



Fig 5

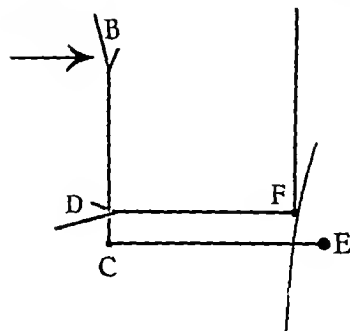


Fig 6

Figs 1 to 5 Steps in method of reducing dislocations at shoulder joint.

Fig 6 Diagram showing mechanics of procedure.

of a lever acting at the point  $D$ . The line  $BC$  represents the patient's forearm which acts as a lever with its power arm  $BD$  and weight arm  $CD$ .

The line  $CE$  represents the dislocated humerus upon which traction is exerted by moving the lever  $BC$  in the direction indicated by the arrow. It will be seen that in this mechanism we have a

first class lever with the fulcrum at *D* and with a power arm *BD* and a weight arm *CD*. The pressure of the operator's hand against the point *B* (which is the patient's hand) in the direction of the arrow will result in traction upon the humerus *CE*. As the traction exerted upon the humerus is obtained through the action of a lever of the first class, with a relatively long power arm the expenditure of only a small amount of force is necessary to effect powerful traction upon the dislocated humerus. Because the energy is so small in amount, the degree of traction on the humeral head can be very carefully and easily controlled.

For the past 4 or 5 years this method has been in use on the surgical service at the Milanospolis General Hospital and in my private practice. It has proved generally satisfactory and has not been attended by any unfortunate complications or results. I believe that this method has several advantages over those now in vogue.

1. It may be used in all cases of dislocation of the shoulder joint even those complicated by frac-

tures of the surgical neck, the tuberosity or the shaft of the humerus or the glenoid fossa.

2. The maneuver may be employed without additional injury to the bone or soft tissue and in fact, often times aids in the reduction of the accompanying fractures.

3. No force is applied to the dome of the axilla and consequently there is no danger of injury to vessels or nerve such as often occurs when the foot is placed in the axilla.

4. The method requires no great expenditure of strength and affords powerful controlled traction without the help of an assistant or special apparatus.

5. The method may be used in many cases without anesthesia.

#### REFERENCES

- KOCHER, THEODORE. Eine neue Reductionsmethode fuer Schulterverrenkungen. Berl klin Wochenschr 1870, 7.  
 STROGOV, LEON A. An easy method of reducing dislocations of the shoulder and hip. Med Rec 1900, 37 336.

## OSTEOMAS OF THE NASAL ACCESSORY SINUSES

WITH REPORT OF A CASE ILLUSTRATING THE TRANSCRANIAL APPROACH TO ORBITAL STRUCTURES

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**O**STEOMAS of the nasal accessory sinuses are microscopically benign tumors as they do not invade the surrounding tissues by cellular extension. They do, however, invade, destroy by pressure erosion, and displace neighboring structures by their gradual growth. The symptoms and signs produced by these osteomas depend upon their location and size. The only cure for them at the present time is complete surgical removal. When considered from this standpoint, they not infrequently present problems of considerable magnitude. In order to prevent complications which might result in death or to conserve the function of neighboring organs and prevent unsightly deformities, a careful study is required to determine their origin, structure, situation, and extent. Originating as they most commonly do in the nasal accessory sinuses, they may invade the cranial cavity, the orbit, the nasal cavity, the bones of the face, and other sinuses. If the tumor is so located that there is obstruction to drainage from the nose or accessory sinuses, secondary infection is likely to result and this may complicate both the clinical picture and the operative technique.

## LOCATION AND FREQUENCY OF OCCURRENCE

Fetisoff (5) collected 258 cases of osteoma of the nose and sinuses. Those arising from the sinuses were distributed as follows:

Frontal sinuses, 131, or 50.7 per cent, ethmoidal labyrinth, 69, or 26.7 per cent, maxillary sinuses, 16, or 6.2 per cent, sphenoidal sinuses, 8, or 3.1 per cent. Thus osteomas originate more frequently in the frontal than in all the other paranasal sinuses. Many times these tumors involve more than one sinus and may be multiple themselves. They should be classified according to their point of origin rather than by the space they occupy or their direction of growth, but this site may be difficult to determine after growth has reached a large size.

## ETIOLOGY AND PATHOLOGY

In another more recent article by Fetisoff (4) on the pathogenesis of osteomas of the nasal accessory sinuses, the usual microscopic classification of these tumors is followed, i.e., they are grouped, according to the type of osteoid tissue

found, namely, eburnated, spongy, and mixed forms. After a review of the literature and a careful study of 4 cases, he arrives at the following conclusions: First, that the growth of the osteoma takes place from the inside outward by the metaplasia of fibrous tissue into bone tissue, second, that the osteoplastic ossificatory process takes place at the periphery of the osteoma and plays a secondary rôle in the growth of the tumor, third, that the fibrous tissue filling the inter-spaces of spongy bone is a direct continuation of the periosteum covering the osteoma from the outside, fourth, that the theory of origin of osteomas from the periosteum split off at the stage of the development of the organism is the most fundamental. This author believes also that the presence of split off periosteum at the early stage of development of the organism is not yet sufficient for the appearance of the tumor. He further states that, according to the recent theory of development of tumors, an exterior irritant is necessary, apart from the power of the cells, to produce tumor growth. Trauma and inflammatory processes in the nasal accessory sinuses may, undoubtedly, play the role of the exterior irritant in the development of an osteoma. There is evidence of this in the history of the majority of cases.

Grossly, the osteomas are usually irregular or nodular. They may be partially covered by the mucous membrane of the sinus in which they arise. There is also a periosteal covering. Many case reports emphasize the hardness of the bone and the difficulty which is encountered in attempting to remove it with the usual bone instruments. The spongy type, however, is easily excavated. The pedicle of attachment is usually small and easily separated. It may however be broad and firm.

## AGE AND SEX

Adolf Lebert-Möbius reports the sex incidence in 180 cases of osteoma as follows: males, 110; females, 70. Of the age incidence given 102 of 103 cases were less than 30 years of age, while 61 were over 30. It is probable, however, that in many under 30 and especially those of greater age than 30, some had had the tumor a number of years. For instance, Cumston states that cases are known



Fig. 1. Mrs. J. Picture previous to operation showing the outward, downward, and forward displacement of the right eye.

of 15 or 20 years duration and that he has knowledge of one which has been present for 43 years. Many cases are seen from puberty to the age of 20. These years cover the time in which the sinuses develop most rapidly and is most opportune for the development of osteomas.

#### SIZE AND RATE OF GROWTH

From the preceding paragraph one realizes that the osteomas may be very slow in growth, their development usually being couped by years. It is also generally conceded that the growth is more rapid in younger individuals. The larger growths are usually found to be microscopically of the spongioid type and are considered the more rapidly growing. The very hard, ivory like tumors are usually smaller and are more slowly growing. Osteomas have been described as weighing as much as a pound but the larger ones are very rarely found in this age of surgery.

#### EXTENSION OF THE GROWTH AND RELATED SYMPTOMS

The orbit is by far the most common cavity attacked outside the sinuses themselves. The symptoms and signs produced by invasion of the orbit depend upon the degree of invasion and the location from which it takes place. Exophthalmos is the most common and prominent sign of osteoma of the sinuses with orbital invasion and, because a large percentage of these cases arise from the ethmoidal and frontal sinuses, the growth extends into the orbit from the superior or medial aspect or the angle between the superior and medial aspects. This results in displacement of the eye downward, outward, and forward. Should the invasion take place from the lateral

or the inferior walls of the orbit, the displacement of the eye is medially and upward.

There may be considerable displacement of the eye without apparent or very little disturbance of vision. Pressure or tension on the optic nerve may interfere with vision. If pressure is exerted against the muscles of the nerves to the muscles, oculomotor palsies may result. If the circulation is interfered with, there may be an ischemia or papilledema of the retina depending upon whether the obstruction affects primarily the arterial supply or the return venous flow. Should the eye be pushed forward so far that the lids fail to cover the globe, corneal ulceration and its complications are likely to ensue. Also inflammatory conditions in the nose and sinuses may find their way along the growth and cause a similar reaction in the orbital tissues.

In osteomas arising from the frontal and ethmoidal sinuses, if the direction of growth is upward and backward, erosion of the bony wall of the cranial fossa takes place and the tumor becomes partially intracranial. Displacement or perforation of the dura with pressure upon the frontal lobe may eventuate without symptoms as long as no complications occur. However perforation may release cerebrospinal fluid, which passes along the growth and drains by way of the sinuses and the nose. Infection may thus occur by this route and produce brain abscess or meningitis. Cushing reported 4 cases of osteoma, in one of which cerebrospinal rhinorrhea communicating with the cerebral ventricle took place. In a second there was a huge intracerebral pneumocele while in a third there was found an intradural pneumocele. Two of his cases were further complicated by infections and the patients died of meningitis and brain abscess.

The most frequent cause of disaster following the surgical removal or attempts at surgical removal of these tumors has been intracranial infection. This must be considered of prime importance when the cranial cavity has been entered and especially when the dura has been opened.

When osteomas invade the nasal cavity the symptoms are those of obstruction, loss of smell and discharge. Obstruction frequently is complicated by infection due to improper drainage. If the growth is limited to the sinuses, in which no obstruction to drainage takes place usually no symptoms occur. However when obstruction is present a mucocoele may develop, or infection may occur. The obvious symptoms are the result of these secondary changes. An osteoma may be found with ease on routine examination for



Fig 2 Roentgenogram taken in the occipitofrontal position



Fig 3 Roentgenogram taken in the lateral position

other conditions in which the tumor produces no symptoms whatsoever. If the growth is large enough, all the neighboring cavities may be affected by a single tumor, i.e., the frontal sinus, the ethmoids, the nasal cavity, the cranial cavity, and the orbits.

#### PAIN AND HEADACHE

Pain and headache are found only occasionally in the presence of osteomas. Many patients with large tumors have never been disturbed with either symptom, and it is probable that headache or pain does not occur except as follows: (1) when there is pressure on a sensory nerve, (2) when secondary infection is present, (3) when drainage from the sinuses has been obstructed, (4) when an intracranial complication has arisen.

#### DIAGNOSIS

The diagnosis of an osteoma of the sinuses, if of appreciable size so that it has displaced other organs, can scarcely be mistaken for other growths if an X-ray is taken. However, in 1 case Cushing mistook the lesion for an ossifying meningioma. It is possible for a growth to occur about the orbits in which bone formation or calcium deposits may occur. In the main, careful X-ray studies must be relied upon for diagnosis of the lesion.

#### PROGNOSIS

Among the reported cases in which patients were not operated upon, a mortality of 48 per

cent due to complications is recorded (A. Eckert-Mobius). This, no doubt, is far too large, as only the more severe and complicated cases are of sufficient interest to report. The operative mortality has been estimated at from 7 to 10 per cent. The location and extent of the tumor is of the utmost importance in the prognosis. Small tumors located in the frontal, ethmoidal, and maxillary sinuses should be removed without difficulty and with practically no mortality, while tumors located in the sphenoids may be practically inaccessible and the danger of surgery may be so great that one is not justified in attempting removal. Tumors which invade the cranial cavity are the ones in which complications following operation have most frequently ended fatally.

#### SURGICAL CONSIDERATIONS

The only method that will produce a complete and permanent cure of the condition is the careful radical removal of the tumor, together with its pedicle and a portion of bone from which the pedicle is derived. The eburnated or sclerosing type may not recur when broken from its attachment, even though the pedicle remains. The mixed type and especially the spongy type is prone to recur if separated in this manner. Therefore, one should plan an operative procedure which will give sufficient exposure not only to remove the tumor together with its site of origin but will also



Fig. 4

Fig. 4. Picture taken 9 days after operation showing some improvement in the displacement of the eye.



Fig. 5

Fig. 5. Picture taken 20 days after operation showing



Fig. 7

the scar within the hairline and the use of the rubber tissue drawn through the incision.

Fig. 7. Photograph of the tumor removed at operation.

enable one to deal with any complication that may arise from its position and location. This is especially true in the tumors that penetrate the

cranial cavity. One should conserve, in so far as possible, the function of the neighboring organs, especially the eye. Also, it is desirable to prevent deformity and unsightly scars. It is obvious that where there is such a variation in size and position of the growth, each case will demand planning that is applicable to its peculiarities. In a large proportion of cases reported previously, the exposure has been either that which is used by ophthalmological surgeons for investigating the orbit or the one employed by rhinologists for external operations upon the paranasal sinuses, with such modifications as the particular tumor necessitated. In 1917 Cushing proposed a new method of exposing osteomas which projected into the cranial chambers, producing intra-cranial complications.

#### INDICATION FOR OPERATION

Since there is great variation in the final result of cases in which operation has not been done, namely, a course which may proceed without symptoms or one which may terminate in death, it becomes necessary to determine the possible or probable course before deciding on the type of treatment. Hence if a small encephaloma or osteoma is discovered during the course of an examination by roentgenogram of the head and if present in a young individual, it might be checked up in from 4 to 6 months time. If there is then noticeable an increase in size or in symptoms, operative treatment should be instituted. If the tumor occurs in an adult, a much longer time might elapse before checking it up with X ray for as a rule, they grow much slower in an adult than in youth. They may never require treatment.

Should a similar tumor be found and be thought to be of the spongioma or mixed type, due to its

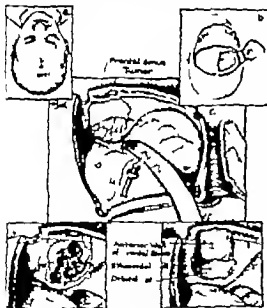


Fig. 6. The skin incision and location of the bone flap, b, the skin flap turned forward and the bone flap raised with pedicle of temporal muscle, c, detailed view showing the dura retracted from the posterior frontal sinus wall and the roof of the orbit, with the tumor in the frontal sinus outlined behind the wall of the sinus and the orbit. The needle is placed in the orbit to release tension, d, the area exposed by the bone drill, e, the resulting cavity after the tumor was removed. The anterior wall of the frontal sinus is somewhat eroded by the growth, the orbital fat arched in the position formerly occupied by the tumor and an ethmoidal cell is unoccupied. The nasal frontal duct is open.

poor calcification, it should be observed more frequently and again operative intervention should be considered upon increase in the size of the growth or if symptoms are produced by it.

When a patient presents himself with a well developed tumor which is causing deformity, exophthalmos, obstruction of the nose or nasal sinuses, with resulting infection or mucocele, or with an intracranial complication, the indication for operative treatment is already present and one need not delay other than to prepare the patient in such a manner as will render him a suitable operative risk.

Cushing's method of approach is that commonly used in operations upon the pituitary in which the anterior cranial fossa is entered over the roof of the orbit by turning down toward the temporal fossa a full thickness flap and retracting the dura. This gives a wide exposure of the roof of the orbit and dura overlying the ethmoidal and frontal sinuses, and will permit the repair of the dura by suture or the application of a fascia transplant. After the dura has been repaired the tumor can be attacked by removing the roof of the orbit or the orbital wall of the ethmoidal and frontal sinuses. This approach, which may be called a transcranial exposure of the orbit, besides giving an exposure through which the dura may be adequately repaired makes it possible to retain the supra-orbital arch of the frontal bone. This prevents deformity which would result from the removal of the bone which forms the arch. It is also possible to remove a large growth upward with less trauma to the orbital contents.

Naffziger's (6) operation for decompression of the orbits in progressive exophthalmos uses a similar approach. He employs a transverse incision above the hairline to hide any scarring. The scalp is turned forward and a bone flap made as in a transfrontal approach to the pituitary. When infection is present, the method of Cushing permits better drainage and the flap may be left open until the infection is cleared up and secondarily closed.

The transcranial approach to the orbit has seldom been described. It gives an excellent exposure from the orbital arch anteriorly to the sphenoidal ridge posteriorly and is applicable for exposing any tumor in the upper portion of the orbit as well as in the floor of the anterior cranial fossa. This approach was chosen in the case to be reported (1) because the attachment of tumor was evidently on the cranial wall of the orbit and frontal sinus, (2) because complete removal necessitated the exposure of dura (3) because it was felt that there would be less disturbance of the



Fig. 8 Photograph which was taken 50 days following operation, at which time the hair had covered the scar of the original incision and the eyebrows had grown in. There is practically no ptosis of the right upper eyelid and the globe is not noticeably displaced.

orbital content, (4) because there would be no visible scar, and (5) because the orbital arch would be preserved, preventing deformity which would occur if the growth were attacked from the usual anterior approach. The latter would necessitate removal of the supra-orbital arch and anterior wall of the frontal sinus, leaving some scarring and make a plastic procedure necessary to correct the resulting deformity.

#### CASE REPORT

The patient, a shoe factory worker, was a woman aged 20 years. She came to the Clinic on December 7, 1933, stating that she believed her eyes had been prominent for the last year. She felt nervous and tired easily. She had been told that her condition was due to goiter. Her family history was negative and her past history revealed good health on the whole although she had had a tonsillectomy for tonsillitis and an attack of abdominal pain for which an appendectomy had been performed. She had no other symptoms except an occasional headache and diplopia after prolonged use of her eyes or when she became fatigued. During the past year she felt that she had been more nervous, tired more easily and was much more irritable than previously but in spite of this she had gained 15 pounds in weight.

Her general physical examination revealed a well developed and nourished woman of 20 with a pulse rate of 90 regular in rhythm and a blood pressure of 120 systolic and 80 diastolic. The chest including the heart and lungs was found to be normal on examination. The same was true of the abdominal, the rectal and the vaginal examinations as well as that of the extremities and of the reflexes. The special thyroid examination showed unilateral exophthalmos (Fig. 1), some nervousness and instability but no other signs of toxicity while her thyroid gland was normal in size and consistency. The ears, nose and throat were

quite normal with the exception of acid retching attacks.

The laboratory report revealed a negative blood Wassermann and the blood counts and urinalysis were within normal limits. The examination of the eyes showed the right globe to be displaced forward, laterally and downward. There was good function of all the muscles in spite of the displacement and there was diplopia only when the muscles are fatigued. There was moderate ptosis of the right upper lid. The ophthalmoscope disclosed no abnormality of the fundi. Palpation under the right orbital ridge revealed an irregular, amenable tumor of bony hardness. X-rays of this area showed an outgrowth of the frontal sinus apparently originating on the nasal wall of the sinus and the orbit. The tumor extended forward and downward into the orbit and frontal sinus, and also upward.

When the sinus, the size and location of the growth are illustrated in the X-ray and drawing (Figs. 4 and 5). Consultation was held with the Neurosurgical Department and the transnasal approach to this tumor was agreed upon as being the most feasible for the reasons already mentioned.

The patient entered the hospital December 1, 1934, and was prepared for operation the following day. The anterior half of the head and the eyebrows are shaved and prepared as for intracranial operations. The combination of local, ether, and ether anesthesia as given. A long coronal incision is made when the hairline from the left temporal region over the scalp and down the right temporal region, as illustrated, and the scalp is pulled forward over the forehead down to the supra-orbital ridges. A frontal bone flap was then outlined on the right side (Fig. 6) similar to those used for pituitary tumor exploration. This flap was turned down, about difficulty in the usual way. The temporal fascia and muscle formed a good pedicle. The dura was intact and slightly tense. A such as made in the upper portion and a sterile needle introduced to relieve tension.

The dura was now retracted from the roof of the orbit and the orbit was found to bulge upward more than in the normal case. In the course of turning down the flap, the upper portion of the frontal sinus had to be opened and the osteoma could be seen to be present as illustrated. Beginning with the upper portion of the sinus, its posterior wall was removed as far as possible with the rongeur, so that portions of the medial part of the osteoma were exposed. It was impossible to carry this very far, however, because of the fact that the tumor was attached to the posterior wall of the sinus and, therefore, intimately adherent in this region. The motor burr as then used to drill into the roof of the orbit (Fig. 6d) removing bone to which the osteoma was attached. After this had been accomplished, it was possible to lift the growth backward as it was not adherent elsewhere. The osteoma was grasped and lifted up and, breaking off the orbital tissue from its irregularities.

The neck in the dura was closed. The overhanging edges of the posterior wall of the frontal sinus were removed as well as its lining membrane in the upper and outer portion. This area of the sinus was obliterated by allowing the dura and brain to come forward. The mucous membrane in the medial portion and in the region of the nasal frontal duct was not disturbed and probe could be readily passed into the nose. The roof of one ethmoidal cell had been removed. Its membrane was not disturbed.

All bleeding points were controlled. The bone flap was put back into place and the pericranium. As advised around the bone flap to hold it firmly. The scalp was then turned upward into place and the closure made in layers, leaving small rubber tissue drain at each end of the incision.

Immediately following operation the head of the bed was somewhat elevated and the patient was cautioned against blowing the nose to prevent forcing air into the region formerly occupied by the frontal sinus. As further precaution she was given 1/4 of morphine hypodermically. Otherwise, the pain and headache were relieved by aspirin and pyridium. Local anesthetic as sufficient to give rest for the night. The eyes were dressed with 1 per cent boric acid solution. No other care as necessary except the dressings. The usual postoperative course was quite uneventful. The temperature reached 100 on one occasion. Otherwise, it fluctuated between 98 and 99. There was great deal of edema of the scalp and face which rapidly disappeared and was practically normal by the fifth day. The drains were removed on the second postoperative day and all wounds are out by the third day. There was considerable drainage of serum through the ends of the wound. The patient was allowed up on the sixth postoperative day and as discharged from the hospital three days after operation.

The patient returned to her work in a month and Figure 8 shows the result 50 days after operation. She also reported for check up on October 6, 1934, months from the time of her operation. She was quite well in every respect and the right eye appeared to be back in the normal position.

## BIBLIOGRAPHY

1. Cushing: *Internat. Clin.* 9:20, 33.
2. Cushing: *Surg. Gynec. & Obst.* 62:747, 748.
3. Leuten: *Monatsh.* A. *Handbuch der Hals-Nasen-Ohren-Heilkunde* by A. Denker and O. Kahlert Vol. 5, p. 8.
4. FERNSTEDT: *Ann. Otol. Rhinol. & Laryngol.* 1930, 38, 404-41.
5. Idem: *Ann. Otol. Rhinol. & Laryngol.* 1932, 41, 333-340.
6. NAYLOR: *Ann. Surg.* 93, 94, 483-50.
7. Idem: *J. Am. Surg. Soc.* 93, 40, 16-7.
8. Idem: *West. J. Surg.* 93, 40, 530-43.



A USEFUL DIAGNOSTIC SIGN IN VERTEBRAL INJURIES<sup>1</sup>

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THE literature in recent years reviews a strikingly large number of vertebral injuries which have not been recognized until a very late stage when the condition has become irreparable. In a series of 90 cases of fracture of the spine, Stewart reported that 31 per cent of the fractures were overlooked. Fumagalli and Christopher found similar large percentages. These facts are unfortunate because, with the method of treatment by hyperextension, the results obtained in recent cases are fairly satisfactory. Early diagnosis, therefore, is obviously a necessity for the elimination of deformity and the reduction of permanent disability.

The diagnosis of vertebral fracture is frequently overlooked for several reasons. At the time of injury the clinical picture is clouded by damage to muscles and ligaments, which gives diffuse pain and extensive muscle spasm. The symptoms of fracture, on the other hand, may be extremely mild in character, and the patient is treated conservatively until, with disability persisting, a roentgenogram is taken which reveals the true pathological condition. The mechanism of the trauma may itself be of such slight degree that suspicion of the vertebral damage is not aroused. This is well illustrated by one of our cases in which the mere mechanism of stooping to pick up a light piece of wood produced a compression fracture of the twelfth dorsal vertebra without evident pre-existing pathological change. Another patient in our series, aged 38, fractured the third lumbar vertebra doing her habitual, but very active, morning exercises.

Often in patients with multiple fractures, such as are commonly seen in modern automobile accidents, the picture of shock and the problems of reduction of fractures in the extremities distract the surgeon's and the patient's attention so that the spinal injury is not recognized until the patient is ambulatory. In our series there are several patients, who were seen by us long after injury, who belong in that group. Diagnosis is usually made clinically by pain, limitation of spinal motion and tenderness, symptoms and signs which are generalized and which may be the result of other lesions than a vertebral injury. Frequently, in order to execute the routine examination of the back, the patient must be moved about and handled in a manner which is not only painful but sometimes harmful.

For several years we have employed a maneuver which is extremely helpful in the diagnosis of vertebral injuries. Although it is exceedingly simple, results can be obtained only if every detail of its technique is observed. The patient is placed flat on his back without pillows, the examiner places one hand upon the sternum of the patient exerting a slight pressure so that no flexion can take place either at the lumbar or dorsal regions of the spine, at the same time the examiner's other hand is placed under the occiput and with this hand the head is bent upon the neck, then slowly but forcibly, the head and neck are flexed upon the sternum (Fig. 1). This produces a progressive pull upon the posterior spinous ligaments, starting at the ligamentum nuchæ and being transmitted downward to the interspinous ligaments until it reaches the spinous process of the injured vertebra. On this it acts as a lever gently compressing the body and producing pain which the patient localizes very accurately (Fig. 2). The role of the interspinous ligaments is illustrated by Case 2 of our series. This man had a fracture dislocation of the first lumbar vertebra and presented a positive neck flexion test well localized at this area. A laminectomy was performed to relieve pressure on the cord, and following this procedure this test became negative. Watkins, in a paper on low back pain published in 1931, described briefly but accurately, this maneuver as the "Soto-Hall sign." Following a personal communication from us he had employed this test and mentioned its usefulness. Munzer, in 1933, described a head-bending test which he found valuable in inflammatory, trau-

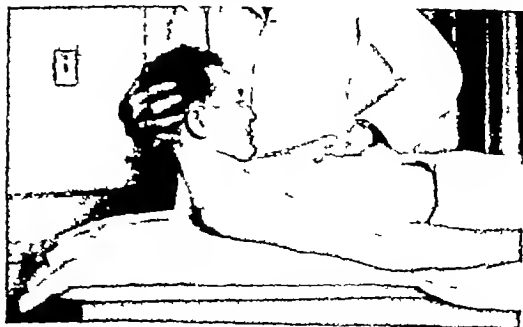


Fig. 1 The maneuver used to detect vertebral injuries

<sup>1</sup>The experimental part of this paper was conducted under a grant from the Christine Breon Fund for Medical Research of the University of California

TABLE I.—RECENT FRACTURES OF SPINE—UNDER ONE MONTH

Age	Sex	Age	Interval since injury	Symptoms and signs	Roentgen diagnosis	Neck flexion test
	F		day	Tenderness over lumbar spine and pain	Fracture of spine L	Positive
	M		do	Asymmetry of legs	Fracture of spine with cord compression	Positive over L, test became positive at once following lumbarotomy
	F	37	day	Lypsis, low back pain	Fracture of spine L	Positive over L
	F		days	Tenderness over L 1	Fracture of spine L	Positive over L
	F	34	day	Severe low back pain	Fracture of spine L	Positive over L, still positive four years later
	M		day	Tenderness over lumbar spine	Fracture of spine D 12	Positive over L
	F	33	do	Tenderness over D	Fracture of spine D 10	Positive over D
	M	43	day	Tenderness over cervicolumbar	Fracture of spine D and	Positive over D 15
	M	47	day	Tenderness over D and	Fracture of spine D and	Positive over D and
36	M	38	days	Tenderness over L and	Fracture of spine L	Positive over L
37	M	39	day	Tenderness over and dorsal	Fracture of spine D 8	Positive over D
38	F	30	day	Tenderness over D and	Fracture of spine D	Positive over D
	M	30	day	Tenderness over low lumbar	Fracture of spine L	Positive over L
	M		day	Tenderness over mid lumbar	Fracture of spine L	Positive over L
	M		week	Tenderness over lower dorsal	Fracture of spine D	Positive over D
44	M	30	days	Tenderness over mid lumbar	Fracture dislocation of spine L	Positive over L and
	M		weeks	Tenderness over mid dorsal	Fracture of spine D	Positive over D
48	M	33	weeks	Tenderness over cervicolumbar	Fracture of spine D	Positive over D
49	F	30	month	Pain over right scapula	Fracture of spine D	Positive over D
50	F		month	Lumbar back pain	Fracture of spine L and	Positive over L

Total number of vertebral fractures  
Percentage, positive neck flexion test

30  
100

matic, and various neurological disturbances, and believes that this head bending test is positive when the roots are involved as in infectious myelodysplasia.

We have employed this sign in a large number of cases during the past 4 years and have tabulated a series of 58 consecutive cases in order to determine its value in differential diagnosis. To facilitate this evaluation we have arranged these cases in the form of tables showing the relationship of the neck flexion test to the clinical and radiological findings (Tables I to V). The sign was found to be uniformly present (100 per cent) in patients with recent compression fractures of a vertebral body which could be demonstrated by the X-ray. It has been our experience that a negative test within a month of an injury to the back was conclusive evidence of the absence of vertebral fracture. A well localized positive test is strongly suggestive of such an injury, but may be found in other acute conditions. In carrying out this maneuver one should not interpret as positive test the discomfort and tightness near the

cervicodorsal junction of which some patients complain.

In cases of acute sprain of the back, we have found a small percentage, consisting of the more severe ones, in which the sign is positive. In these it was noted that the pathological changes were mainly in the lumbosacral area, whereas most sacro-lumbar sprains gave a negative sign. This sign is also positive in vertebral tuberculosis during the active stage and in tumors when some damage has occurred to the body of the vertebra. We have not followed a sufficient number of these cases of tuberculosis or tumor to determine its value in diagnosis, or its worth in estimating healing or the prognosis, which should be studied.

When injuries to the back are so commonly found associated with medico-legal problems, it is important to attempt to elicit information by methods which do not involve directly the suspected region. In such cases this maneuver has great value since information can be obtained without attracting attention by local examination of the injured area.

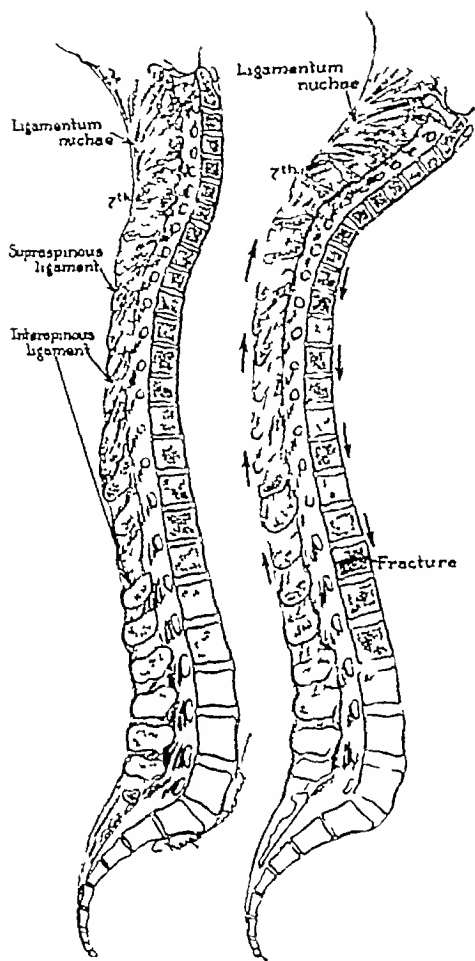


Fig 2 A drawing explaining the maneuver

#### EXPERIMENTS ON THE TRANSMISSION OF IMPULSE FROM THE CERVICAL SPINE TO THE DORSOLUMBAR JUNCTION

To obtain experimental confirmation of the previously described clinical observations, a series of experiments was carried out on three rabbits. These experiments were performed along similar lines and with identical results, so that only one of the series need be described. A large male rabbit was killed with ether, the skin and superficial fascia were removed from the back and fine needles were inserted into each of the spinous processes from the third dorsal to and including the first lumbar. The animal then was firmly attached to a wooden board by means of a nail driven through its pelvis and other nails placed

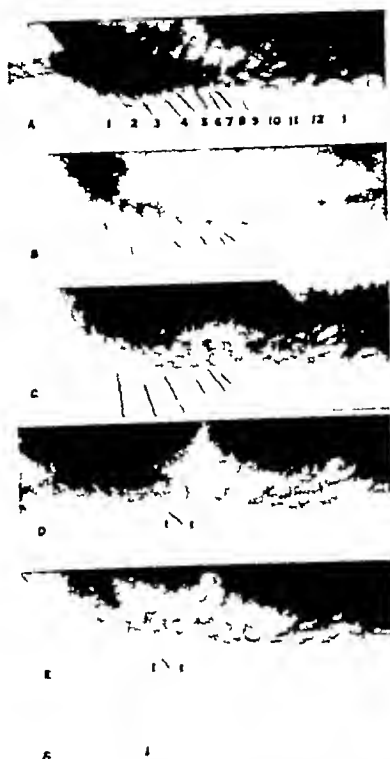


Fig 3 A, Neck extended B, Neck flexed C, Neck flexed, back muscles removed D, Neck extended, back muscles removed, ligaments cut between T3-T4 and T4-T5 E, Neck flexed Same as D

just anterior to the vertebral bodies in the cervico-dorsal junction and in the lumbar region. Further immobilization of the dorsolumbar region was accomplished by the firm pressure of a piece of wood extending along the dorsal surface of the animal. Without changing the position of the thoracic or lumbar region, the following procedures were carried out and roentgenograms were taken.

**Procedure I** The neck was extended (Fig 3 A). The neck was then flexed (Fig 3 B). Upon carrying out the latter maneuver the spinous processes in the dorsal region showed a progressive separation in the manner of the opening of a fan, which movement was demonstrated more clearly by the excursion of the needles which had been inserted in the spinous processes.

**Procedure II** The muscles of the back were removed on both sides of the spine. The neck then was flexed as shown in (Fig 3 C). Movement occurred in the spinous processes and the corresponding needles in the same manner as in Procedure I.

TABLE II—SPRAINS OF BACK

Case No.	Sex	Age	Duration of symptoms	Signs and symptoms	Clinical diagnosis	Neck flexion test
21	M	47	day	R1 sacro-diac tenderness	R1 sacro-diac sprain	Not painful
	M	49	day	L4 sacro-diac tenderness	L4 sacro-diac sprain	Not painful
	F	49	day	L sacro-diac tenderness	L4 sacro-diac sprain	Pain over L4 sacro-diac
22	M	37	day	R1 lumbar tenderness	R1 lumbar muscle sprain	Not painful
	M	39	day	Lumbosacral pain	Sprain of superior sacral muscle	Not painful
23	M		day	R1 sacro-diac tenderness	R1 sacro-diac sprain	Not painful
27	M	49	day	Lumbosacral pain no tenderness	Lumbosacral sprain	Not painful
28	M	39	day	L4 sacro-diac tenderness	L4 sacro-diac sprain	Not painful
29	M	38	day	R1 lumbar pain	R1 lumbar muscle sprain	Not painful
30	F	37	week	Tender over 4th lumbar	Lumbosacral sprain	Pain over 4th lumbar
	M	34	weeks	Tender over lumbosacral	Lumbosacral sprain	Not painful
31	M	33	weeks	Tender over R1 sacro-diac	R1 sacro-diac sprain	Not painful
32	F		weeks	Lumbar pain and tenderness	Lumbar muscle sprain	Not painful
34	M	34	month	Tender over sacro-diac	R1 sacro-diac sprain	Pain over sacro-diac
35	M		month	Tender over D 8 and 9	M8 dorsal sprain	Not painful
36	M	44	year	Tender over sacrum and upper thighs	Sacro-pelvic sprain and neural degeneration	Pain over sacrum
37	M		6 weeks	Right coccyx pain	R1 sacro-diac sprain	Not painful
38	M	42	weeks	Lumbosacral pain and tenderness	Lumbosacral sprain	Pain over lumbosacral
39	M		months	Lumbosacral pain and tenderness	Lumbosacral sprain	Pain over lumbosacral
40	F	32	16 weeks	Tender over L2 sacro-diac	L2 sacro-diac sprain	Not painful
41	M	36	months	Tender over R1 sacro-diac	R1 sacro-diac sprain	Not painful
42	M	38	months	L4 tender and sacro-diac pain	L4 sacro-diac sprain	Pain over R1 sacro-diac

Total number of cases 42  
Percentage positive neck flexion test 33

TABLE III—ARTHRITIS OF THE SPINE

Case No.	Sex	Age	Duration of symptoms	Signs and symptoms	Clinical diagnosis	Neck flexion test
43	F	45	month	Tender over C1 and upper dorsal	Arthritis of spine of upper dorsal	Pain over C1
44	M		months	Lumbosacral pain	Arthritis of spine L1 and 2	Pain over lumbosacral
45	M	40	months	Rapid spine lumbosacral	Arthritis of spine lumbosacral	Not painful
46	M	30	8 months	Tender over D 8, 9	Arthritis of spine dorsal	Not painful
47	F	43	years	Backache tender over D7 and 8	Arthritis of spine, mid-dorsal	Not painful

Total cases 5  
Percentage positive neck flexion test 40

Procedure III All the posterior ligaments between the third and fourth dorsal vertebrae were cut down to the cord also between fourth and fifth, as shown by arrows in Figure 3 D and E.

Following the severance of these ligaments it was seen that flexion of the neck produced a separation of the spinous processes only as far distally as the fifth dorsal vertebra, beyond which no movement occurred (Fig 3 E).

Procedure IV A laminectomy was done at the

level of the third and fourth dorsal vertebrae. Flexion of the neck then produced a slight movement of the fifth dorsal vertebra, which movement no longer occurred after the bodies of the second and third dorsal vertebrae were removed. The spinal cord shifted slightly cephalad on flexion of the neck.

#### EVALUATION

The foregoing procedures indicate that the movement of flexion of the neck causes a tension

TABLE IV—TUBERCULOSIS OF THE SPINE

Case No.	Sex	Age	Duration of symptoms	Signs and symptoms	Clinical diagnosis	Neck flexion test
43	M	28	3 months	Pain and kyphos at D 7	Tuberculosis of spine, D 7 and 8	Pain over D 7. Test became negative 15 months after Hibb's fusion
49	M	54	6 months	Pain in back paraplegia	Tuberculosis of spine D 10 and 11	Pain over L 1
50	F	10	1 year	Scoliosis tender rt. sacro-iliac	Tuberculosis of spine D 12	Pain over L 2
51	F	24	1 year	Tender over L 3 and 4	Tuberculosis of spine, L 3 and 4	Pain over lower lumbar. Test became negative 1 year after Albee fusion

Total cases 4  
Percentage positive neck flexion test 100

TABLE V—MISCELLANEOUS

Case No.	Sex	Age	Duration of symptoms	Signs and symptoms	Clinical diagnosis	Neck flexion test
52	M	28	1 day	Tender over lt. costovertebral angle	Fractured arthritic spur on D12	Pain over L. border of L 1
53	M	28	5 days	Pain over mid lumbar	Fractured arthritic spur on L 3	Pain over L 3
54	M	60	6 months	Kyphos and tender over D11 and 12	Metastatic carcinoma of spine D12 and L 1	Pain over D 11 and 12
55	F	26	3 months	Low dorsal pain and tenderness	Contusion of back	Not painful
56	F	68	3 months	Tender interscapular swelling	Contusion of back	Not painful
57	M	24	1 week	Mid-dorsal tenderness and kyphos	Osteochondritis of spine	Pain over mid-dorsal
58	M	39	5 months	Tender over D 4	Kummel's posttraumatic syndrome	Pain over D 4 dorsal

Total cases 7  
Percentage, positive neck flexion test 71

upon the ligamentum nuchæ, the supraspinatus ligament, and the interspinous ligaments by means of which a progressive slight separation of the spinous processes of the dorsal region accompanies flexion of the neck. This takes place in the absence of the muscles of the back. The amount of movement, however, is greatly limited after the excision of all ligaments. An almost negligible motion of the vertebræ occurs as a result of the transmission of the impulse through the vertebral bodies.

To summarize, these experiments give an explanation of the fact which has been observed clinically and reported in the accompanying tables namely that flexion of the neck, mainly by the transmission of ligamentous pull, causes pain which is localized at the level of the injured vertebral body when it is the site of a compression fracture or destructive process.

## SUMMARY

The usefulness of this sign rests upon the following facts

1 It gives the exact location of recent fractures without moving or disturbing the patient

2 It guides the technician in obtaining roentgenograms at the proper level

3 It aids in the differentiation between the injury of bone and damage to soft tissue

4 It is helpful in medico-legal cases because it does not attract the attention of the patient to the lesion and he is not aware of the area that is being tested

5 A negative test almost eliminates the diagnosis of recent vertebral injury

6 Confirmation of the clinical observations is given by experiments on rabbits

## REFERENCES

- 1 CHRISTOPHER, F. Compression fractures of the spine. *Am J Surg*, 1930, 9: 424-429.
- 2 FUMAGALLI, C. R. Le fratture misconosciute del rachide. *Clin. Chir.*, 1928, 31: 1291-1317.
- 3 MÜNZER, F. T. Zur Symptomatologie der Hinterwurzelaffektion (das "Kopfbeugungs-Symptom"). *Med. Klin.*, 1933, 29: 945-946.
- 4 STEWART, L. F. The frequency of unrecognized fractures of the vertebral column. *Penn. M J.*, 1929, 32: 695-697.
- 5 WATKINS, JAMES T. Low back pain—one of the commonest human afflictions. *Better Health*, 1931, 12: 131-138.

## A NEW OPERATIVE PROCEDURE FOR BRACHIAL BIRTH PALSY— ERB'S PARALYSIS

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SEVERAL operations have been used for correcting the internal rotation deformity of Erb's palsy and so improving the position and to a certain extent the function of the shoulder. Among these are the section of the subscapularis tendon devised by Sever, the rotation osteotomy of the humerus devised by Hubbs, and the subperiosteal rotation of the humerus by Kleinberg. All of these correct the deformity but in a sense are negative operations; that is, they do not attempt to restore the action of the deltoid except indirectly. It was in an attempt to do this that the operation here described was devised.

The majority of cases of brachial birth palsy are of the upper arm type and in these there is usually considerable power left in the deltoid. It was noted that in these cases the anterior portion of the deltoid is frequently almost normal in power while the posterior portion is practically powerless. The operation to be described is an attempt to utilize a portion of this strong anterior deltoid to reproduce more nearly the normal deltoid action, by restoring the balance between the anterior and posterior portions. To accomplish this a portion of the origin of the anterior deltoid is shifted backward to replace the paralyzed posterior portion and by thus changing its direction of pull, restore the normal deltoid action at least in part.

**Technique.** The patient lies on the operating table with the shoulder to be operated on elevated by a sand bag placed well under the scapula. The incision commonly used is transverse, extending from about the middle of the spine of the scapula to a little beyond the anterior end of the acromion process. This incision reaches the ridge of the scapular spine behind and the lateral portion of the anterior half of the deltoid. At times the anterior end of the incision is extended down and along the muscle for an inch or two. The superficial fascia is stripped back from the muscle for a distance of 2 or 3 inches, but the muscular sheath is not disturbed. The next step is preparation of a bed in the spine of the scapula for the reception of the transplanted portion of the deltoid. This is done by splitting the periosteum over the ridge of the scapular spine at about the place where it begins to spread out into the acromion process medially for about  $\frac{3}{4}$  inches.

The periosteum is then stripped from both sides of the scapular spine and a portion of the bone of the spine is gouged out. Next the portion of muscle to be transplanted is prepared. Care must be taken to take good healthy functioning muscle. We have been able to secure sufficient by cutting off the outer border of the acromion process with the attached muscle. The process being cartilaginous is easily divided with a knife or sharp osteotome. After separating the tip of the acromion the deltoid muscle is split downward along the course of the fibers by blunt dissection. Care must be taken not to divide too far downward in order not to interfere with the nerve supply of the remaining anterior portion of the deltoid. It seems to be safe to divide it approximately half way from the acromion process to its insertion in the humerus. At this stage of the operation the floor of the incision is formed by the capsule of the joint and if the subscapularis muscle is tight, it can be divided as in Sever's operation. This has been necessary in some cases. After the muscle strip has been prepared, the arm is abducted laterally and externally rotated to allow the separated acromion, with the strip of muscle attached to be fitted into the bed prepared in the scapular spine. It is then attached by chromic catgut sutures to the spine of the scapula. The periosteum stripped from the spine is also sutured to the edges of the separated portion of the acromion with chromic catgut. The arm must be held in the abducted and externally rotated position from this point on through the application of the cast. Closure of subcutaneous tissue is done with catgut and the skin with silk worm. A cast over the body and arm is then applied with the arm in the position mentioned.

The cast is left on 6 weeks, after which the portion over the shoulder and arm is blivaled and the upper portion removed, the rest being left as a splint. The patient then exercises the arm by moving the elbow and raising it from the splint. After a week the body portion of the cast is also blivaled so that it can be removed for increased motion of the shoulder and replaced. After weeks it is completely removed. At this time the humerus is held fixed in abduction on the scapula, somewhat as in a shoulder fusion. This will be

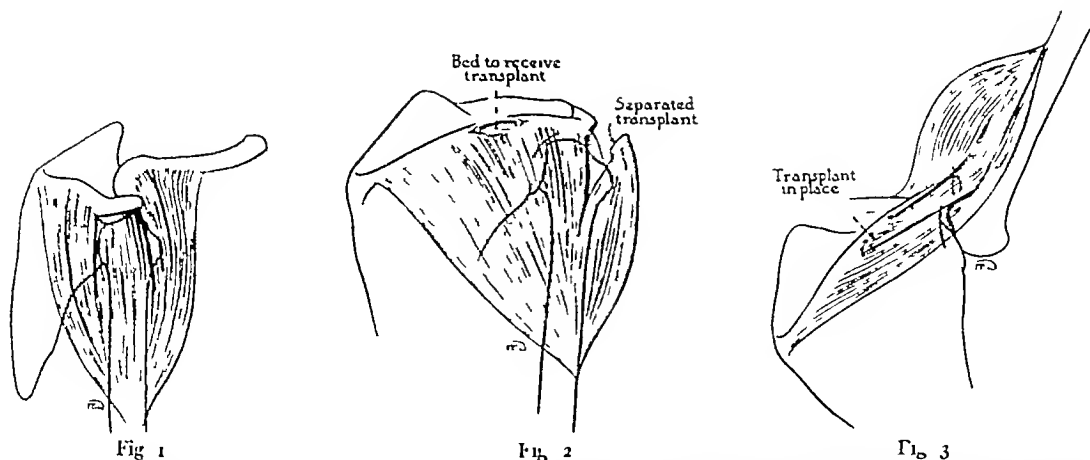


Fig 1 Diagram showing portion of deltoid to be transplanted

Fig 2 Diagram showing transplant separated and bed prepared in scapular spine

Fig 3 Diagram showing transplanted muscle sutured to scapular spine. Humerus abducted and externally rotated

attributed to the fact that the transplant is somewhat short for its new position. We have felt that it was better to let the necessary adaptive lengthening take place gradually rather than to attempt to hasten the process by stretching. The length of time for this varies but usually takes 2 or 3 months. The transplanted muscle seems to act as an external rotator largely and this gives the principal improvement in function of the arm.

The operation, of course, is of no value in cases with complete deltoid paralysis. Its field is limited to those cases in which the anterior deltoid is strong, and in these it has been effective in restoring the muscle balance to a certain extent.

We have had one flat failure. This we ascribed to the fact that the child was too young at the time the operation was performed. The tissues were very soft and it is possible that the transplant did not hold. Also he was too young to co-operate successfully in exercises.

The operation has been done on 7 patients, all at the Shriner's Hospital.

CASE 1. R. H. aged 13 years was operated upon January 6, 1930. The patient had the usual internal rotation deformity of the shoulder. In this case there was a definite backward subluxation of the humeral head from the glenoid cavity. Passive motions of the shoulder joint were quite free. i. e., there were no contractions of the subscapularis or pectoralis. There was some flexion contracture of the elbow joint from the biceps contracture. The humerus was somewhat shortened. Active abduction of the shoulder laterally was nil anteriorly to a right angle. In this case the subluxation of the humeral head attracted attention and in trying to think out a means of preventing it, transplantation of a portion of the deltoid backward

suggested itself with the idea of reinforcing the posterior portion of the joint capsule. On removal of the cast the improvement in function was so noticeable that it seemed wise to try the procedure on other cases. In a way the improvement in the shoulder function was a by product. This patient was last seen April 24, 1934. He can now abduct the arm laterally to a right angle and externally rotate it about 45 degrees. To his mind the greatest improvement

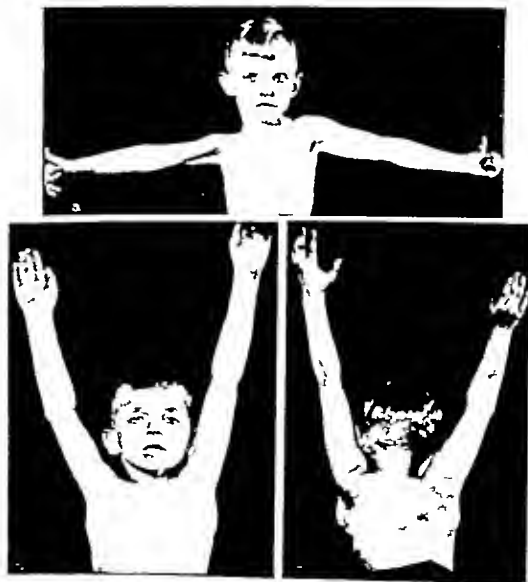


Fig 4 Case 3. C. H. Good result. a, Before operation, showing maximum abduction and external rotation of right arm. b, After operation, showing abduction. c, Back view, showing abduction. Note the shortening of the upper arm and forearm.



Fig 5 Case 4 R. P. Gould result. a, After operation, showing improved external rotation of shoulder. b, Before operation, showing maximum abduction and external rotation of left shoulder. c, After operation, showing improved abduction of shoulder.

so that he can now throw his hand up enough to catch baseball.

Case 2 D. B. age 3 years January 7, 1931 The patient presented the usual internal rotation deformity at the shoulder. Passive motions of the joint are free. Active lateral abduction as about 90 degrees. Anterior abduction was possible to right angle. Lateral rotation was nil. This case is failure, because patient was operated upon at too early an age. The tissues are very soft and it is possible the transplant may not be held.

Case 3 C. H. aged 5 years, as operated upon January 16, 1931. There is the usual internal rotation deformity of the shoulder with moderate shortening of the humerus. Passive motions are free. Active abduction laterally was possible to slightly less than right angle to right angle anteriorly. Lateral rotation as nil. Patient was last seen January 12, 1931, at which time he could raise the arm above his head nearly as far as the normal one. External rotation as 90 degrees.

Case 4 R. P. aged 7 years, as operated upon August 2, 1931. The usual internal rotation deformity with moderate shortening of humerus, as noted. Passive

motions were free. Active motions lateral abduction to right angle— anterior abduction to right angle. External rotation as nil. Patient was last seen June 6, 1931, and could now raise arm practically straight over head. Lateral rotation as 90 degrees.

Case 5 C. P. aged 7 years, was operated upon April 6, 1931, for the usual internal rotation deformity. Passive motion was only slightly limited (head had better operation previously). Active motions—lateral abduction as about 3 degrees, anterior abduction about 60 degrees or less. Lateral rotation was nil. In this case the lower arm was also affected. Hyperextension of the forearm as lost and flexion of the first two fingers as weak. Patient was last seen June 2, 1931, when he could place the hand back of head. Lateral abduction was possible to right angle, external rotation to about 60 degrees. The transplant could be felt functioning.

Case 6 J. K. aged 7 years, as operated upon July 5, 1931. He had the usual internal rotation deformity. Passive motions were considerably limited. Abduction as possible to somewhat less than right angle laterally. Internal rotation as markedly limited. Active motions—



Fig 6 Case 5 C. P. 1st result. a, Before operation, showing maximum lateral abduction and external rotation. b, Before operation showing maximum active anterior

abduction. After operation, showing improved active abduction and external rotation. d, After operation, showing improved active external rotation.



lateral abduction was about 30 degrees, anterior abduction, about 80 degrees, external rotation was nil. On account of the marked limitation of passive movement, a Sever operation was done in connection with the deltoid transplant in this case. Patient was last seen April 25, 1934, when lateral abduction was possible to a right angle. He could rotate shoulder externally enough to place hand on head with shoulder abducted laterally. This patient was one in whom the motion of the shoulder joint was somewhat slow in returning. He has developed a somewhat peculiar technique of using the arm by fixing the head of the humerus with the transplant and then moving the scapula.

CASE 7 J M. Aged 6 years was operated upon October 12, 1933. He had the usual internal rotation deformity. Passive motions were poor. (Had had Sever operation 1 year previously.) Active motions—lateral abduction about 0 degrees, anterior abduction, nearly 90 degrees, external rotation nil. Patient was last seen July 26, 1934. He could then abduct the arm laterally to right angle and could rotate externally enough to place the hand on top of the head. Motion of the shoulder joint was returning, rather slowly.

#### ANALYSIS OF CASES

Of the 7 cases, 3 can be classed as much improved, 3 as considerably improved and 1 as a failure. The more favorable cases for the operation seem to be those in which there is a fair amount of lateral abduction present. In these cases there is at least a fair amount of power present in the portion of the deltoid originating from the acromion. Hence, when this portion is transplanted backward it functions more vigorously. The most noticeable improvement has been in the external rotation. In 2 cases a splint of the usual obstetrical paralysis type was applied for some time after the removal of the cast. In these 2

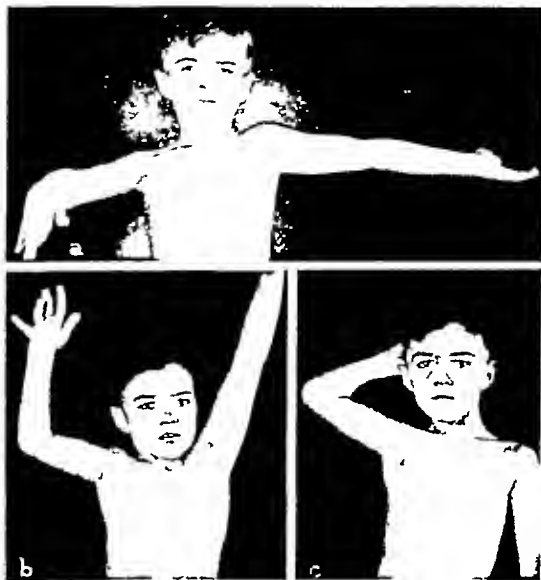


Fig 7 Case 6 J R. Fair result. a, Before operation, showing maximum active abduction and external rotation of right shoulder. b, After operation, showing improved abduction and external rotation. c, After operation, hand placed actively behind head.

cases, stiffness of the shoulder joint was slower in disappearing.

While the series of cases reported is small and too recent to state definitely what the long range result will be, yet the procedure has shown improvement in the function of the arm.

## POSTOPERATIVE OR VENTRAL HERNIA

A METHOD FOR RELIEF OF TENSION AFTER REPAIR

A. R. DICKSON, M.D., F.A.C.S., BATTLE CREEK, MICHIGAN

North Creek, Southwestern

THE procedure about to be described is contributed to the already voluminous literature on postoperative or ventral hernia, with the firm conviction that it will decrease the number of failures of this often formidable operation and will bring some apparently inoperable cases within the field of operability. It can also be used in cases in which because of obesity and high intra-abdominal tension, postoperative hernia is likely to develop. The device may perhaps be crude and amenable to refinements of application, but it is believed that the principle is sound and the method has proved effective in actual practice.

The majority of abdominal incisions are made in the longitudinal axis of the body. They are popular because of the increased ease of exposure over the transverse incision in spite of the fact that this transverse incision avoids nerves and is parallel to the direction of the fibers of the transversalis fascia on which the integrity of the abdominal wall depends. Intra-abdominal tension is horizontal or at right angles to the longitudinal axis of the body. Chiene aptly described it as a tug of war going on between the two groups of oblique muscles of the abdominal wall. It is this constant drag away from the midline of the abdominal wall that puts tension on suture lines used to repair a longitudinal incision, thus causing ischemia of wound edges and necrosis. It also causes sutures to cut through, produces serum in wounds leading to infection, and makes healing difficult and scars defective.

It is much more important to direct effort to relieving wound tension than it is to devise some new type of suture material. A wound that is completely relaxed and without tension will have a good blood supply and no matter what suture material is used, whether absorbable or non-absorbable, or it might almost be said, whether any at all is used, the wound will heal. In practice a moderate amount of abdominal tension is not inimical to wound healing and especially if some tension sutures are so placed as to relieve the strain on the wound margins.

It is in the obese patient, however, with a high degree of intra-abdominal tension that we have our difficulties, and if the hernia is large and is more than likely in the upper abdomen, we have

a situation that often borders on the inoperable and in which there is a high surgical risk and numerous failures. Reduction in weight helps to lessen intra-abdominal tension but such efforts are often only partially successful.

## THE DEVICE

The device here illustrated is a heavy can as belt similar to that long used for fracture of the pelvis. It is wide enough to include the lower ribs and the hips. The ends come to slightly above the level of the abdominal wall and are split into tails so as to more closely follow the contour of the body and prevent all the tension being taken up by the hips and the ribs. A row of small pulleys is attached to either end of this belt and a small sash cord laced through these pulleys after mating with a row of pulleys attached to a metal bar a short distance above the abdominal wall (Fig. 1). The amount of squeezing together of the abdominal wall can be somewhat regulated by the distance of this upper row of pulleys from the abdominal wall. The bar is then lifted by a cord attached to either end and threaded through a pulley and the tension maintained by weights attached to a cord running through pulleys on the overhead frame of a fracture bed (Fig. 2). About 20 pounds of weight is all that has ever been found necessary. The head of the bed can be elevated to

assist the patient a comfort. The patient can turn to either side without increasing the tension on the wound and what is of great importance the wound can be dressed without increasing the strain on the sutures as would be the case if adhesive strapping had to be cut and the abdominal wall allowed to sag to either side. More kindly healing is shown by the lessened amount of serum and infection in the wound.

The purpose of the sling is to lift the weight of the sides of the abdominal wall and also to compress the hernial margins toward the midline. Of the two, the lift is the more important and does the most to relieve tension. The time-honored method of adhesive strapping fails to do this and permits of dragging each wall from the midline. This method also fails to keep up a constant even relaxation of the abdominal wall. The apparatus here described does accomplish this by following

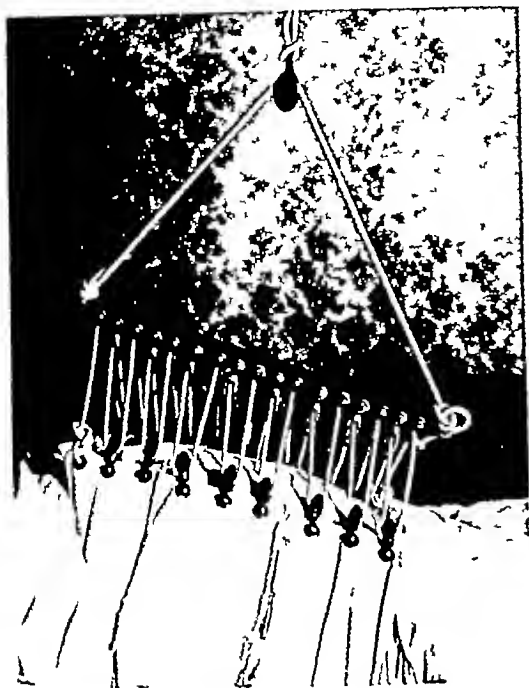


Fig 1

every move of the patient with an even lift as in fracture extension. The efficiency of this method may be demonstrated by strapping an obese abdomen with long strips of adhesive tightly enough to approximate the edges of the ventral hernia. If the patient is then placed in this sling the adhesive can be easily relaxed to a marked degree by a lift of 15 to 20 pounds. The adhesive thus becomes unnecessary.

The early discomfort of which some patients will complain when the apparatus is first put on can be greatly lessened by its application for a week in advance of operation. During this time the patient becomes accustomed to bed regimen and gets over a great deal of the restlessness which is usually present after being first put to bed. The very real danger to life which accompanies repair of large ventral hernias comes largely from the increase in intra-abdominal pressure. This produces pressure on the diaphragm and embarrassment of respiration making hypostatic pneumonia a not uncommon complication. Alarming



Fig 2

cardiac symptoms from pressure on the heart and abdominal vessels are often seen. Acute dilatation of the stomach and ileus may complicate the picture and further increase the pressure. This may all be largely avoided by this period of pre-operative preparation. The abdomen should be strapped with wide adhesive tightly enough to approximate the edges of the hernial ring and reduce its contents into the abdomen. The sling is then applied and enough weights added to lift the abdominal wall and obtain considerable relaxation of the adhesive strapping. Several days should then intervene before operation. The patient then becomes accustomed to the increased intra-abdominal pressure. There should be no embarrassment of heart action or of respiration, no vomiting, and the bowels should be functioning normally, before operation should be considered. If untoward symptoms arise and the patient cannot tolerate this program, it should be a warning that surgical repair is risky or impossible and should thus prove a valuable test of operability.

When this principle was first being tried out this apparatus was applied after the patient had returned from the operating room. Often this increased the postoperative discomfort and pressure against the diaphragm and heart to such a degree that it had to be removed. Since this period of pre-operative preparation has been carried out, no patient has developed alarming post-operative symptoms, for he has become accustomed to the apparatus beforehand, and the post-operative course has been smooth.

## EDITORIALS

### SURGERY GYNECOLOGY AND OBSTETRICS

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DECEMBER, 1935

#### THE MESENTERY

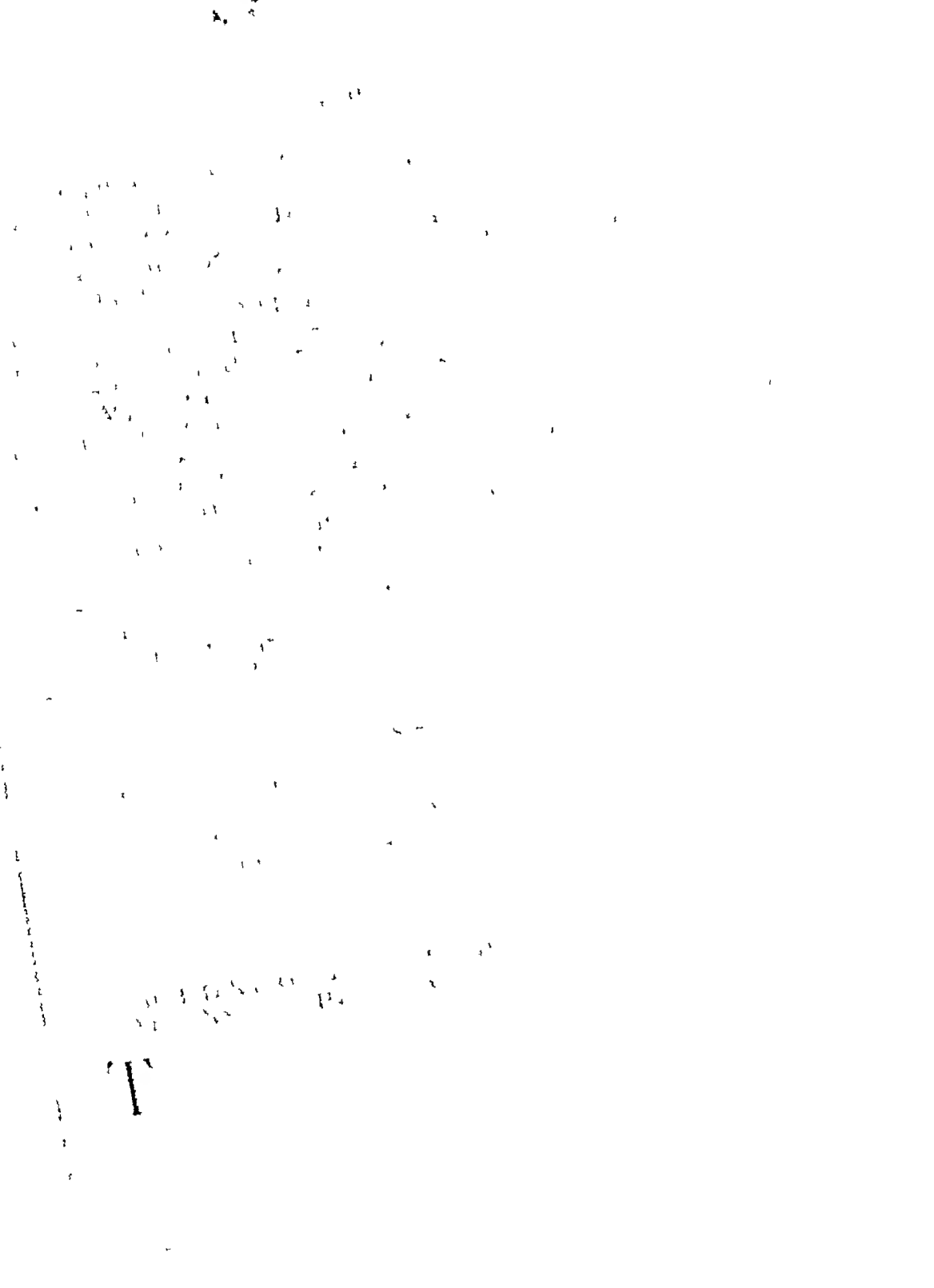
TEXTBOOKS of anatomy devote but little space to one of its most extraordinary and important parts, the mesentery. Casual inspection might give the idea that the mesentery is merely a ligament to maintain the small intestine loosely in its variable position. It is true that the mesentery performs this function, but in so doing an anatomical structure is presented difficult to imitate in human made apparatus. The root of the mesentery or its parietal attachment, where apparently it arises from the posterior abdominal wall, is only 15 centimeters long, whereas its visceral attachment, where its layers divide to enclose the full length of the jejunum-ileum, is nearly 7 meters long. In other words, the mesentery in extending an average of 30 centimeters from its origin to its intestinal attachment increases in length forty-six times, a result attained by marvelous "tucking." Through such a widespread distribution the superior mesenteric artery, entering the mesentery at its root, probably subdivides into more branches than any other artery in the body. Moles description of the arrangement of the vascular loops in

the mesentery is helpful in identifying different portions of the intestine.

Consider then the vital products of digestion which flow through the mesenteric veins and lymphatics—the total output of the chemical laboratory of the alimentary canal. In these vessels, inanimate foodstuffs first take on living properties. Just what biochemical changes occur as aminoacids, sugars, and fats pass through the intestinal wall do not yet seem to be fully explained. The interminable branching of the vagus and sympathetic nerves in the mesentery exerting such significant control of intestinal action is no less wonderful than the vascular supply.

From a surgical standpoint the mesentery is equally interesting and important. Tuberculous involvement of its glands (*tubercles mesenterici*) may simulate tumors or appendicitis, or other abdominal diseases. Lymphosarcoma may be the cause of intestinal obstruction, while obstruction also may be due to volvulus or intussusception produced by defective mesenteric attachments. Again calcified glands in the mesentery may be mistaken for calculi in the kidney or ureter until their mobility under the fluoroscope clears the diagnosis.

The absence of collateral circulation of mesenteric arteries must be constantly borne in mind in operations upon the mesentery and small intestine. If the excision of a cyst menaces the blood supply of a segment of bowel the segment also should be removed. In intestinal excision and anastomosis for trauma or disease disaster will follow failure to preserve vascular integrity. Especial care is necessary in an end-to-end anastomosis



In the presence of the third and fourth degrees of attachment, the clinical diagnosis of malignant disease is usually obvious. Fixation of the second degree is usually easily elicited by physical examination. Often it is difficult to detect attachment of the first degree, because the lesions are small and of relatively short duration and the degree of attachment as has been said depends on the situation of the growth in the tissues of the breast. If the tumor is situated on the posterior wall of the breast, there may be little or no attachment of the skin because the growth is attached to the underlying major pectoral muscle. If the lesion is situated on the anterior surface of the breast attachment of the skin will be noted even if the lesion is very small. If there is a large amount of fat between the growth and skin the fat may become lobulated may give a soft feeling to the tumor and in many instances may lead one to believe that the soft feeling area is larger than the tumor beneath. Tumors situated in the extreme margins of the breast often present unusual physical characteristics because of the difference in the character and distribution of the subcutaneous fat over the breast and over the adjacent thoracic wall.

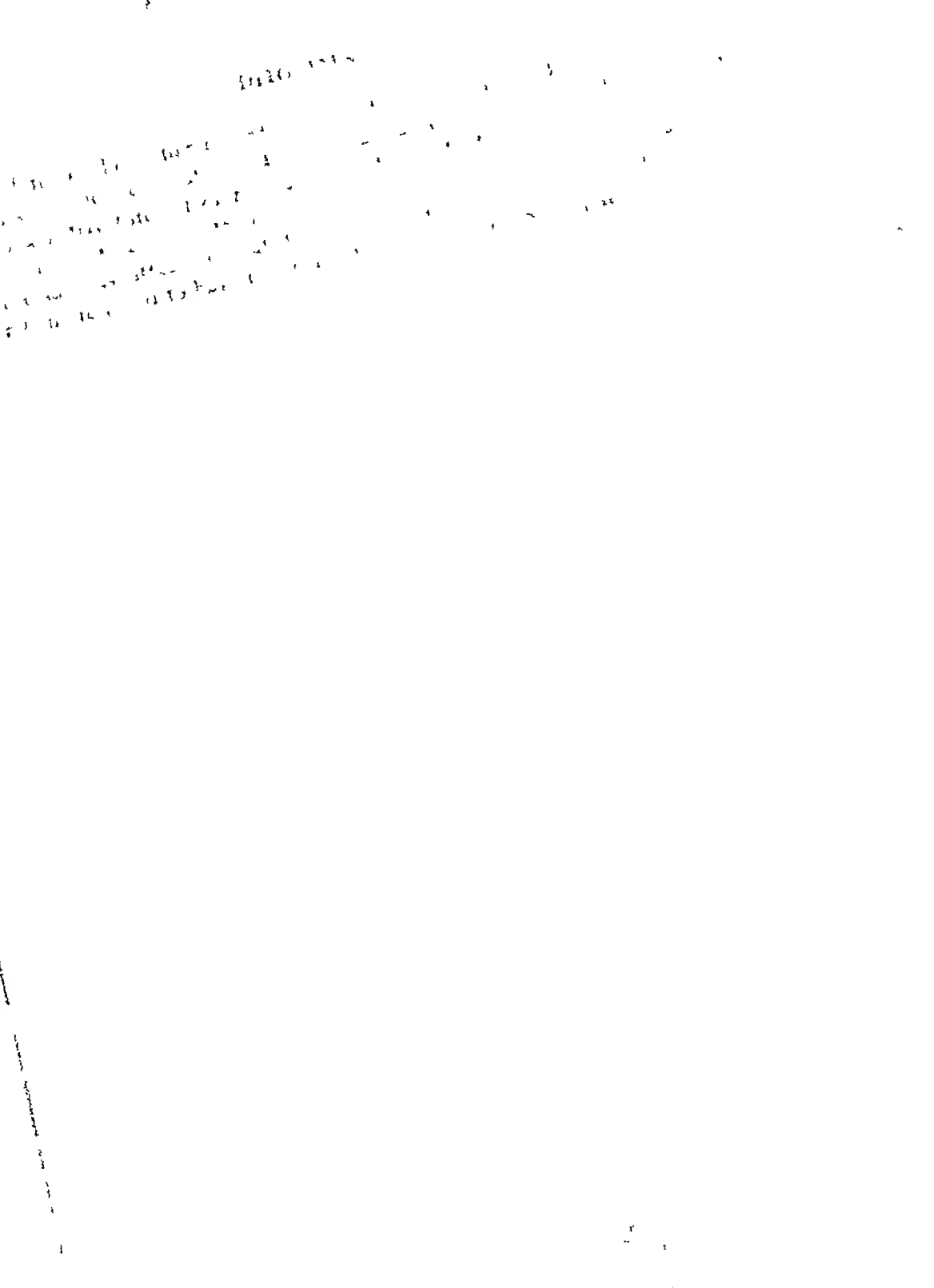
The skin may appear to be attached to benign lesions of the breast because of the fold of skin in the region. Not uncommonly malignant growths along the extreme margin of the breast are not thought to be primary tumors but metastatic growths from lesions elsewhere. This is particularly true of growths situated in a region of accessory mammary tissue high in the axilla.

It is often difficult to detect the presence of cutaneous attachment to tumors that are situated close to the nipple or areola because of the contraction of the muscular fibers of the areola and nipple. These fibers often will make it appear that the skin is attached to

the tumor when in reality such apparent attachment is a puckering of the skin brought about by contraction of the muscle. It is interesting to note the changes in the appearance in many of these cases at the time of operation, after the patient is anesthetized the characteristic appearance of attachment cannot then be elicited because of relaxation of the muscular fibers of the breast.

Attachment of the skin to benign lesions of the breast is usually the same as the first degree attachment of malignant lesions. Cutaneous attachment to benign tumors usually is caused by an inflammatory reaction in the underlying mammary tissue, such as is seen in a region of purulent mastitis, fat necrosis, comedo-mastitis, or in a region of mastitis over a simple cyst. This last is probably the benign lesion that most commonly is diagnosed clinically as malignant disease. The error occurs not only because of the slight attachment of the skin to the underlying mammary tissue as a result of pressure, but also because of the hard, irregular feeling of the tumor as a result of the nodular mastitis that lies between the skin and the cyst. In many instances these cysts are found on the posterior wall of the breast, and when the breast is examined while the patient is leaning forward the rounded contour of the posterior wall of the cyst can be felt. In most instances these tumors are fairly large, and the absence of any enlargement of the regional lymph nodes suggests a benign lesion. A malignant tumor of as large size usually gives evidence of regional metastasis.

The most important malignant lesions of the breast, from a surgical standpoint, are early growths to which the skin is attached in slight degree. Inasmuch as this degree is also found in benign lesions, it is often difficult to make a definite clinical diagnosis on physical examination alone. As has been said



# LANDMARKS IN SURGERY

CARL LUDWIG SCHLEICH

HIS CONTRIBUTION TO REGIONAL ANESTHESIA—AN HISTORICAL RECORD

ALBERT H. FREEMAN, M.D. F.A.C.S. CINCINNATI, OHIO

JUNE 24th was an eventful day for the surgeons of Germany in the year 1892. On this day there was dedicated in Berlin the Langenbeck Haus, erected as the permanent home of the Deutsche Chirurgische Gesellschaft and as the future meeting place of its annual congress. At the invitation of a friend, I was privileged to attend some of the sessions during the dedication and to see in attendance many of those men of Germany whose names have meant so much in the development of surgery and its specialties. Among these might be mentioned Geheimrath Ober Medizinal Rath, Professor Adolf von Bardeleben, chief of the I. Surgical Clinic of the Berlin Charité Hospital, the president of the congress Thierisch, of Leipzig; FRANK KOENIG, then professor at Goettingen, later called to the chair in Berlin and author of that textbook on surgery which, in my opinion, is the best which any German has produced, von Bergmann, James Israel Goltz, who was secretary of the Congress, Trendelenburg, von Eschsch, Max Schuch, Gumboldt, Oskar von Bardenheuer, Riker von Einsleberg, von Mikulicz, of Breslau, Julius Wolff, in whose clinic I was working, a younger man, later Wolff's successor—Albert Hubs, the real founder of a modern group of German orthopedic surgeons, greatly beloved by all who knew him.

A paper which seemed to me of particular interest was that presented at a session on June 1, by Carl Ludwig Schleich, who was announced to speak on "Infiltration Anesthesia (Local Anesthesia) and its Relationship to General Narcosis." Schleich was a young man and rather handsome. According to his own memoirs<sup>1</sup> he was then 33 years old. His attitude was one of quite apparent assurance—perhaps too much so in view of the audience which he was addressing. (As a long time has elapsed since the occurrence of the episode which is being described, I have refreshed my memory by consulting the stenographic protocol which is found in the society's *Proceedings*.) After an introductory section in which the analgesic effect of distilled water and various solutions was set forth, he described the use of very dilute solutions of cocaine in isotonic salt solution dilutions varying from 1:1000 to 1:10000. The approach to the clinical

portion of his paper was then made by the following, which is a fairly literal translation from the official protocol.

Thanks to the perfected development of operative technique which we owe chiefly to our great masters of the pre-scientific period, not least to him whose memorial names this house bears, the dangers of an operation involving technical difficulties such as hemorrhages and traumatic damage may be said no longer to exist, provided there has been good training. Under his ready guidance for us to make the dangers of infection dependent upon our sense of responsibility and care, the danger of infection by asepsis to lay the necessary ground work upon which there remained to be done must especially be replaced the danger of narcosis.

With this statement murmured went through the hall and it was not difficult to read cynicism in the men's faces. The paper concluded with a statement, however, the effect of which can not be entirely envisioned in its verbiage. For this one could require the personal impression which receives vividly with me to this day an impression of great satisfaction with self, of the consciousness that something of permanent value was being handed over to posterity as indeed it was in truth. Schleich's concluding sentence was:

However, I must declare it to be entirely impossible to perform operations under narcosis which might have been done under this or another method of local anesthesia, one not only loses the moral and humanitarian standpoint, but with regard to the criminal responsibility of the surgeon.

The indignation which this final sentence aroused in the president, von Bardeleben, was at once apparent. His florid countenance became suffused with a deeper glow, amounting almost to cyanosis. With evident trembling, he rose to his feet. The auditors were murmuring to one another. The moment was one of great dramatic tension as the president found voice to say:

In my society we are not accustomed to taking votes in matters of this kind. When however such statements are heard at us as contained in the concluding remarks of him who has just spoken, we have a right to express our opinion for the public hearing. I ask those who are convinced of the propriety and truth of the conclusions expressed by him, to raise their hands. Certainly, I observe that no hand has been raised. Is discussion desired?

Immediately there was roaring then which seemed to come from the throats of all of the members. There ensued a period of almost confusion

<sup>1</sup>Monatsschrift für Chirurgie, Berlin. November 1910, 1911.  
Weinberg & Co. Verlag, G. m. b. H., Leipzig, 1911.



in the assembly. It seemed as if everyone present were talking to someone else. The president rang, long and loudly, the large hand bell which stood on his table and which served in place of the chairman's gavel to which we are accustomed. Presently the uproar subsided sufficiently for the president to be heard. He said "Will such as favor a discussion, raise their hands? No hand is raised and there will therefore, be no discussion."<sup>1</sup>

Schleich had advanced to ask for the floor and thus was the occasion for the uproar. There was now nothing for him to do but to withdraw from the hall. As he approached the entrance, there arose from his seat a few rows in front of us a gentleman with a mane of gray hair, who followed Schleich through the door. I learned that this was his father, an ophthalmologist in Stettin, who believed in the statements of his son. It should be added that there was a rumor that the mortality record of the I Surgical Division of the Charité Hospital from chloroform administration was far from good, it was a sensitive point. Even more, it was said that von Bardeleben had had a death from this cause shortly before the meeting.

One year later, at a meeting of the Surgical Society, Schleich was given the opportunity to demonstrate his method. Only 30 men responded by their presence. It was Professor Ernst von Bergmann who extended the invitation, fighter for the establishment of scientific truth that he always was. Aristocratic to his finger tips, von Bergmann was always to be counted on as a virile antagonist to prejudice, to littleness, to niggardly appreciation of merit when questions of scientific and professional advance were involved. And on this very occasion, he did not hesitate to oppose another aristocratic surgeon, von Esmarch.



Carl Ludwig Schleich  
1859-1922

During the years which have followed Schleich's original presentation, his method has become the daily help of surgeon and patient. The essence of Schleich's contribution lies not simply in the idea of fluid infiltration. Halstead had shown, in 1885, what could be done in this manner with distilled water, but the publication consisted simply of a short letter to the editor of the *New York Medical Journal* (September 19, 1885) and it escaped notice on this account. Schleich's contribution was to show the superiority of isotonic salt solution as a medium, on the one hand, on the other, the effectiveness of such weak solutions of cocaine, therein, as had until that time not been credited with usefulness. Upon these two factors, however, the development of all that is now known as "Regional Anesthesia" has rested. To any one who has had experience with regional anesthesia on a considerable scale, Schleich's contribution must be regarded as of great and abiding significance. The use of this method in latter days for the reduction of fresh fractures was enough to establish its great importance—even though it had done nothing else than make it possible to avoid general narcosis in the reduction of recent fractures of the femoral neck, we owe Schleich a great debt. And yet, in a treatise as comprehensive as Labat's work on regional anesthesia, we find only an insignificant allusion to Schleich who so richly deserves credit in this field.

If it be said that Schleich's manner of presenting his valuable contribution has been the reason for the delayed and utterly inadequate recognition by the profession, I am aware that the statement may well be challenged. At the same time, as one who was an eyewitness to the lamentable episode, and as one who has had neither a personal acquaintance with the man, nor any personal interest in him, this is my opinion. The story of the incident is offered as presenting a moral which is too obvious for further comment.

Who hath given man speech? or who has set therein  
A thorn for peril and a snare for sin?  
For in the word his life is and his breath,  
And in the word his death.

(Swinburne, *Atalanta in Calydon* Ode IV)

<sup>1</sup>It may be of interest to add that in the protocol of the session of June 11, 1892, there is found a note which is not mentioned by Schleich in his memoirs. It is in the form of a letter addressed by Schleich to von Bardeleben, in which he says that when he was refused the floor after the reading of his paper he was deprived of the opportunity to dispel a misunderstanding. He did not presume to sit in judgment on the differing opinions of his colleagues concerning the use of chloroform, he was intending to express his own opinion only. But, he maintained, as regarded his own patients that he must replace the dangerous chloroform anesthesia with his own safe method wherever it was possible so to do.

# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

**INFREQUENTLY** books appear that mark epochs in the advancement of medicine. The *hospital organization and management* by Dr. MacEachern is one of these. While many excellent hospitals served the public previously, the last 3 years has witnessed the general evolution of the hospital into a highly organized institution for the care of the sick and the advancement of medicine. In this movement Dr. MacEachern has held a prominent place. His service as a hospital superintendent and later as an official of the American College of Surgeons and other national organizations in the United States and Canada doubtless supplemented by his survey of hospitals in Australia and New Zealand, has given him a comprehension of hospital problems and a group of the details of administration beyond that of any other individual. He has analyzed, marshalled, and compressed this information into readable form and supplemented it with a wealth of practical details in this admirable volume which touches every part of hospital life.

Any individual, group, or community contemplating the organization and building of a hospital will avoid innumerable mistakes and find constructive advice in the chapter dealing with "Promoting and Building the New Hospital," from preliminary organization, surveys of the need, raising of funds, choice of architect, planning the building, contracts, check lists of furniture and non-technical equipment.

The director, the various committees of the governing board, and the various auxiliary staff find their duties outlined and the methods of administering them detailed. The admitting officers will find proper procedure outlined and forms ready made for their use.

The medical staff and interns will be interested in the discussion of their functions and organizations with helpful suggestions as to conference consultations, utopias, the duties of various committees, and their relationships to the patient, the hospital, and the public. Detailed information is given as to the various departments of medicine, surgery, orthopedics, obstetrics, ophthalmology, otolaryngology, and other clinical specialties. His charts for records, check lists for medical and surgical supplies, and diagrams for the advantageous arrangement of units. The adjunct diagnostic and therapeutic department such as laboratories, X-ray physical therapists and

pharmacy will more clearly understand their duties and be helped in their organization and administration. Sample charts for records and reports, and check lists of equipment presented make this chapter invaluable.

The nurse will be interested in the valuable information concerning their education and the care of patients detailed in the chapters dealing with their problems. The superintendent of nurses will find her questions as to the organization and administration of her school and hospital answered in detail. The forms and orders she may need outlined and checked lists of all kinds of supplies furnished. The surgical and obstetrical nurses will be served much time and effort by the procedures outlined and the check lists of supplies and instruments. They will also find comprehensive directions for the proper preparation and sterilization of instruments and the places, and solutions in addition to general discussion of their duties and responsibilities.

The same helpful suggestions with a wealth of detail will be found in the chapters dealing with the dietary, out patient, social service, medical records departments, and all the supplementary service departments such as business, purchasing, housekeeping, laundry and maintenance. Indeed, one is amazed at the wealth of practical information which makes this book an essential in every department of the hospital.

That the cultural and social relations of the hospital are not neglected are evidenced by the chapters on ethics, public education, and the prevailing atmosphere of service and the prevailing here throughout the volume.

This is a book that will be as a permanent contribution to medical and hospital literature. It is educational to laymen helpful to hospital boards, and in an advisable hospital superintendents and personnel not only for the betterment of hospital organization and management but also for rendering more adequate service to the patient. It is a question pertaining to hospitals that could not be adequately answered in the pages of Dr. MacEachern's scholarly work.

**CERTAINLY** for men in all qualified to assist in the treatment of fractures as Dr. Lorenz Roehrer of Vienna. As director of the Hospital for

The Treatment of Fractures, Dr. Lorenz Roehrer, M.D., is the author of this book. It is a practical guide to the treatment of fractures and is a valuable addition to the library of every surgeon. It is published by the Medical Book Co., New York, N.Y.

A B A

Accidents in that city, he is in a position to treat or supervise the treatment of all the common, as well as the bizarre injuries to which bones and joints are heir. He has gathered material representing 19 years of practice in traumatic surgery, and in 560 pages, augmented by 1,009 clear illustrations and many groups of statistics, has presented his thoughts and experiences in this subject. Ernest W. Hev Groves, of Bristol, England, has translated the work from the original German into English and has done so in a succinct, if not staccato, manner that is practically devoid of any redundancy. The style is not flowing but terse and to the point, and it is doubtful if more information (whether or not it is acceptable to all readers) could be had in the given space. The book is approximately 7 by 11 inches in size and is bound in blue cloth. The paper, printing, and reproductions of illustrations leave nothing to be desired.

The book is divided into three parts. Part I, entitled "General," takes up the broad subjects of after-treatment, apparatus, and dressings, application of plaster, treatment of compound and infected fractures, and also deals with operative treatment and the subject of non-union. In general the practice of the author in the management of these phases of fracture work conforms to the methods current in this country. Naturally, however, there are personal variations with which many of our authorities could not concur. As an example, one might mention the treatment of the open wound in a compound fracture with tincture of iodine, and the infiltration of the tissue contiguous with the contaminated field with local anesthetic.

Part II, entitled "Special Fractures and Dislocations," deals with the entire skeletal system beginning with the skull and ending with the phalanges. In this large group, of course, many controversial grounds are entered, and, going over these points critically, one might not always agree that the author's method is the one of choice in all parallel situations. However, in his treatment of these subjects Boehler speaks freely of methods that he has tried and discarded as wanting, and statistical tables offer valid reasons for their abandonment.

The third part of the book is composed of four subtitles appearing under "Appendices." These are (A) statistics, (B) the knee joint and its movements, (C) the position of the forefoot in flat foot, club foot and claw foot, (D) fractures and the surgery of accidents in relation to their environment.

In almost all of the subjects treated the normal is used for comparison, both in text and in illustration, and the requisites for the treatment of each condition are clearly outlined. Common mistakes in the case of each fracture are also enumerated. One experienced in this work might possibly resent the didactic manner in which treatment and mistakes are outlined, but for those who see fractures only occasionally it is probably an apt thought.

The chapter on the os calcis, rewritten and enlarged as the result of recent follow up data, should be cited for special merit. It is based on studies of

the normal mechanics of this bone and its articulation. Practically all methods of closed reduction are explained and statistics presented to show their comparative value in the author's hands, open correction, either as the primary treatment or to rectify a poor result, is touched upon only in passing. It might be added that throughout the book as a whole little space is given to the actual open methods many times required in the treatment of fractures.

Organization of a clinic where such work is done, adequate assistance, and the possession of mechanical appliances are stressed. No bibliography is found, and but few citations of other work in this field are noted in the various chapters. It is decidedly one man's opinion, and of little value from an encyclopedic view. This statement is not to be construed as in any sense derogatory, for the opinion of a man with Boehler's background in this field is definitely of value.

The entire book is readable, logical, and honest, and to be recommended without reservation.

JAMES K. STACK.

IN a single volume of 1111 pages and 1169 illustrations, Hinman has so well organized and outlined the contents of his book on urology that one is readily able to get required information with a minimum of effort. The arrangement of the material makes the book a valuable reference work for the general practitioner and surgeon as well as the urologist. The contents cover all phases of medical and surgical urology as it is understood today. Controversial questions are discussed, and, while the author gives his personal views, he does not dogmatically close the issue.

The first chapters on comparative anatomy, embryology, and physiology are outstanding and simplify certain clinical features which have sometimes been difficult to comprehend readily. An adequate discussion of endocrine activity in the development of the genito-urinary organs and their diseases is given, together with the modern conception of vitamins.

The subject of pain as a symptom is discussed in general. The various types of pain are described in detail and anatomical charts are used which give the scientific basis by which the causes of various obscure pains associated with genito-urinary diseases may be more easily recognized. An excellent discussion is given of anuria in all of its phases including types, causes, and treatment.

The clinical phase of urology logically begins with a detailed examination of the patient and the methods used are presented in outline. General and special features of examination are also included.

Under the headings "Anomalies," "Obstructions," "Infections," and "Lithiasis," general urological diseases are discussed in an original manner, which makes for better continuity of thought, especially when the book is used by medical students.

Under the heading Obstructions, the various types of chronic vesical neck obstructions are described in logical order and the various types of treatment—surgical, electrical, radiological, and roentgenological—are discussed.

Under Infections, the social and medical problem of gonorrhea is covered in detail, and the various clinical and therapeutic aspects of the problem are treated in a comprehensive manner. The sections devoted to pathogenesis and pathology of the various non-specific kidney infections are worthy of mention as is the section on renal tuberculosis.

The subject of urinary lithiasis is presented in greater detail than would be expected in a single volume work, all factors bearing on etiology, diagnosis, and treatment of the various types being thoroughly covered. The treatment of renal stone, including prophylaxis, is worthy of special mention.

In special sections, injuries, tumors, and neurogenic influence of the urinary organs are fully discussed. The female urethra is given attention commensurate with its importance in modern urological practice. Recent studies, directing attention to the many lesions of this structure together with their medical and surgical management, are presented. A noteworthy feature is a complete and scientific discussion of enuresis and urinary incontinence.

Hizman's book is a very complete, modern treatise on urology which should be of value not only to the general practitioner and urologist but as a reference work to the medical student. HARRY COLVER.

THE previous edition of Zondek's work on the endocrine glands appeared in 1926. This third edition in 1935 translated into English, is unquestionably one of the most important additions to the library of endocrinology. It might be said that it is at present the most valuable single volume on this subject. It is less ponderous than an encyclopedic work; it is more extensive than an outline; it is more detailed and thorough than a popular presentation. One-fifth of the book is used for theoretical considerations and physiology. The hypotheses arranged are stimulating; the physiological review is rapid but adequate and contemporary. It is significant that English and American work is given full credit. The clinical studies composing the remainder of the volume are profusely illustrated with short case reports drawn from the author's long experience. Not enough space, however, is given to bio-assay methods in the clinic. In the future it is to be hoped that improvement of assay methods will put clinical endocrine diagnosis on an exact basis. At present, as this book unfortunately shows, diagnosis is largely by inference from body build and non-specific metabolic measurements. In this sense then, this is an old fashioned book but it does contain a large amount of valuable material presented in an informative manner. A classified alphabetical bibliography is appended. PAUL STARR.

THE DISEASES OF THE URINARY ORGANS. By Margaret Zondek, M.D. 2, 770 pp. and col. Translated by Carl F. Henrich, M.D. M.B.C. 5 (May 1, 1935). C.F. (Lancet). Baltimore: William Wood & Co., Inc.

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